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FEB 20 REC'D

Tertre, 4 février, 1991

16456

REF.:
REF.:

FD910112/DH

ETHYL CORPORATION
D. LYNAM, PhD
Director, Air Conservation and
Industrial Hygiene
ETHYL TOWER
451 Florida
BATON ROUGE, LA 70801
U.S.A.

Dear Dr. Lynam,

Re: Toxicological study performed at SEDEMA during 1982-83

Please find hereafter our opinion concerning air concentrations of manganese prior to and at the time of the study.

From 1976 on, SEDEMA had several important increases of capacity in the ore storage, preparation, milling and roasting sections together with facilities producing new salts and oxydes.
Those new processes and equipments were built using best technologies available at that time.
On the other hand, those facilities were added by area extension and this could not lead to raising exposure.

Simultaneously, manpower in the manganese plant went from 111 people in 1976 to the level of 147 people in 1982 and years of exposure have been taken into account in the study.

We consequently consider not correct the assumption meaning that occupational exposures were lower before the study.
This opinion is shared today by Prof. Lauwerijs himself

Hoping the above statement answers your concern regarding Mn air concentrations and exposures at SEDEMA, we remain

Sincerely yours,

F. DELLOYE
Process - Environnement

M. FAUTSCH
Director
Industrial Development

cc: C. Shaper-Chemetals

sedema
GECHEM

sedema
DIVISION DE SADACEM S.A.
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Prof. R. LAUWERYS

Brussels, February 14, 1991

FEB 25 REC'D

Dr D.R. LYNAM
Director
Air Conservation and Industrial
Hygiene
Ethyl Corporation
451 Florida Street
Baton Rouge
LA 70801
U.S.A.

Dear Dr Lynam,

Regarding the intensity of past exposure to manganese in the manganese oxide and salt producing plant surveyed in 1986, I can state the following. As indicated in our paper, no environmental monitoring data were available to characterize the past pollution of the various workplaces. However, although the plant has expanded since it started production in 1964 and although the number of workplaces has increased, the production processes have remain identical and the workers have always performed the same types of activities. Hence, I am enclined to believe that the exposure of each worker has not drastically changed with time and the airborne concentrations of manganese measured during the survey are likely to be representative of the past environmental pollution. This was also the opinion of the chief foreman.

Do not hesitate to contact me, if you need additional information.

Yours sincerely,

Professor R. LAUWERYS

ATTACHMENT 2

Modeling of Manganese Exposure in Mobile Populations

Prepared for

Ethyl Corporation
Health and Environment Department
451 Florida Street
Baton Rouge, LA 70801

Prepared by

Gerald E. Anderson
Arlene S. Rosenbaum
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101 Lucas Valley Road
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Contents

Modeling of Manganese Exposure to Mobile Populations

INTRODUCTION

This report provides a description of studies of community exposure to airborne manganese that were reported on, initially, in less detail in an oral presentation and in the printed proceedings of an EPA workshop[1] held to review potential risks associated with the widespread use of manganese-containing motor vehicle fuels.

Background

The Ethyl Corporation has proposed to market a gasoline additive, HiTEC®3000, that contains methylcyclopentadienyl manganese tricarbonyl (MMT). The Ethyl Corporation and the EPA each have been evaluating potential environmental consequences of the emission to the atmosphere of manganese compounds that result from the use of HiTEC®3000 in motor vehicle fuels. One concern in these evaluations has been that combustion products of HiTEC®3000 emitted to the atmosphere might constitute a toxic hazard to people exposed to downwind concentrations of motor vehicle exhaust products.

Response to this concern has been addressed through studies of the species, forms (gas, aerosol, etc.), and rates of emission of manganese in motor vehicle exhaust; the transport and fate of these emissions that might produce human exposures; and the toxicity of the ingested or inhaled material. This report addresses the transport, fate, and exposure issues only.

---

[1] Manganese/MMT Conference and Health Symposium, Sponsored by the EPA and the NIEHS, Research Triangle Park, NC, March 12 - 15, 1991

The EPA prepared a staff report (EPA 1990), including estimates of "typical" and "severe" exposures. The EPA estimates were based on the analysis of assumed daily activity patterns of prototype individuals that were thought to experience "typical" and "severe" exposures.

To examine the effect of addressing more details in the estimation process, Systems Applications, International (SAI), under the sponsorship of the Ethyl Corporation, undertook a computer modeling study of human exposure to motor fuel related manganese emissions using an actual major urban area (Los Angeles) as a study region and relying on data for input to dispersion, indoor/outdoor, and population mobility modules.

Scope of the Study

The SAI study reported here addressed the dispersion of manganese-containing aerosols emitted by urban traffic and the exposure of various population subgroups as well as of the population as a whole. The dispersion and exposure analyses addressed diurnal variations in the distributions of meteorological events and of the locations (as affecting the degree of sheltering) of exposed people. Only air (inhalation) exposures were addressed, no modeling of dermal or oral exposures from material deposited on surfaces was done; therefore, only air concentrations were modeled; no estimates of particle deposition were made.

Summary of Findings

The exposure of community and sub-group populations to motor vehicle related manganese was studied through the application of a computer model, SCREAM II (Hayes, et al, 1990), to emissions, populations, and environmental conditions in the South Coast Air Quality Management District (SCAQMD, i.e., the Los Angeles region.) Specific results were:

- The estimated mean community exposure compared closely with estimates made by the EPA staff and by other Ethyl consultants and staff, using other approaches.

- The mean incremental SCREAM II inhalation concentration from motor vehicle

emissions, (i.e., without background or "garage" exposures) was 0.009 $\mu g/m^3$. [1]

- Exposures to different age-occupation groups varied by over 50 percent, because their different daily activity patterns favored different micro-environments at any given hour of the day.

- The lowest exposures were to people who spent the most time in controlled atmospheres (e.g., newer commercial or office space). Home environments are less controlled, on average, and thus provided less protection.

- People in the most exposed areas of the SCAQMD receive about twice the mean exposure.

APPROACH

Exposure Pathways

The estimation of human health risk from potential emissions of motor fuel related manganese proceeds from an estimate of the manganese entering the body of an individual or a population. The major routes of exposure to airborne material are by direct inhalation and by dermal absorption or oral ingestion of material, once airborne, that has deposited on solid or water surfaces. Deposited material may enter the body by direct contact with or ingestion of soil or by eating or drinking food or water contaminated by its contact with contaminated soil or biota. The analysis reported here addressed only inhalation exposure.

---

[1] The EPA staff report included an estimate of exposures within a garage micro-environment for "typically" exposed people. It was our impression that few cars in the SCAQMD are parked in an enclosed garage. Also not all A-O groups would use a car daily from its parking place. Thus, this effect was thought to be minimal for this exercize and was not addressed. Estimates were made for home and commercial garages using the EPA method with some data changes; viz., the engine was not idled after park, the driver leaves the garage two minutes after shutoff, and only 12% of fuel Mn is emitted. With these assumptions, the mean daily home garage exposure would be about 0.0001 ug/m3, commercial garage exposure would be about 0.0003 ug/m3.

Deposition of Particulates

Although the material emitted from the combustion of HiTEC°3000 in motor vehicles is in particulate form, deposition rates were judged to be small enough that surface concentrations would be small and dermal and oral exposure routes would not be important. The issue of the importance of these alternate routes for children (who may receive greater doses than adults because of tendencies to have dirty hands and place them in their mouths) was addressed by a work group at the EPA's Manganese/MMT workshop. The group report to the workshop was that the routes were unlikely to be significant, even for children, because significant concentrations would not build up from deposition on surfaces for many centuries.

Inhalation exposures may occur with either gases or fine (inhalable) particles. On the basis of advice from Ethyl staff, it was assumed that manganese emitted from the tail pipe was in the form of a bi-modal distribution of particles. The bi-modal distribution comprises fine particles of less than one micron diameter and considerably larger particles of poorly defined sizes. The larger particles greater than 10 microns diameter are judged by the EPA to be "non-inhalable"[1]. Also large particles would tend to fall out of the atmosphere near the point of emission. Thus, large particles contribute little to inhalation exposure of the community population.

Particles of less than one micron, once emitted into the atmosphere, are carried by the wind and dispersed in a gas-like manner. EPA regulatory models (cf. EPA 1987) treat Total Suspended Particulates (of diameter up to a few tens of microns) by the same dispersion algorithms as gases. The ISC includes an algorithm to model the deposition process, but for particles of a few microns or less, the "settling velocity" is nearly zero[2] and the "reflection coefficient" is nearly

---

[1] Note that the EPA NAAQS for particulates was changed to consider only particles of less than 10 microns. This was done on the basis of inhalability.

[2] At a particle radius of 1 micron and a specific gravity of 2, the ISC algorithm yields a settling velocity of 0.00024 m/s. At this velocity, the reflection coefficient cannot be distinguished from unity in Fig. 2-8 of the ISC user's manual (EPA 1988).

equal to unity; therefore, the loss of material from the atmosphere is negligible, while small, but finite, deposition rates may be estimated.

SCREAM Modeling

The EPA analysis of potential manganese exposure was based on the aggregation of exposure by a prototype person during the course of a day in which time was spent in various "micro-environments"[1]. Concentrations in each micro-environment were estimated using hand calculations with algorithms recommended in a paper by Ingalls and Garbe (1982). While the approach seemed appropriate for a screening analysis, more detailed methods, with more reliance on data, were available for application to this problem.

Systems Applications had recently completed the development of the latest in a line of human exposure models that began with the development of the Human Exposure Model (HEM, [SAI 1983]) for the EPA's OAQPS. The new model, South Coast Risk and Exposure Analysis Model (SCREAM II), developed for the Planning Department of the SCAQMD, incorporated many features that paralleled the EPA approach to estimating manganese risk. SCREAM features include the following:

- Long-term (annual) averaged concentration patterns for each hour of the day estimated using Gaussian plume algorithm for point sources and a modified Hanna-Gifford "box" model for distributed area sources; alternatively, using any specified pattern (e.g., from an EPA UNAMAP model or from monitoring data.)

- Deposition patterns for particulate material computed using default California model, or user supplied module.

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[1] A micro-environment is a space such as a home, office, automobile, playing field, garage, etc. in which the concentration of a certain pollutant bears a characteristic relationship to that in the ambient outdoor atmosphere or in which the concentration depends on internal sources (e.g., concentration in a garage depends on emissions from a motor running in the garage.)

- Dispersion meteorology from data from each of 33 SCAQMD stations, averaged for each hour of the day; data for each source or source zone accessed automatically from proper station.

- Concentrations and exposures specific for each US Census Block Group[1]. In the SCAQMD version of SCREAM, computations are also made at individual city blocks, Census Tracts, or counties.

- Exposures specific for each of 56 population cohorts (aggregated into 12 age-occupation groups for display of results), considering the following:

  - Commute travel by hour of the day between Regional Statistical Areas (RSAs, e.g., sub-regions of the SCAQMD.)

  - Daily Activity Patterns (DAPs) defining their presence in particular micro-environments for each hour of the day.

  - Exercise level in each activity of their DAP.

  - Modeled hour-by-hour concentrations in each of 11 indoor or outdoor micro-environments.

- Multi-pathway exposures[2], following material deposited on the surface through soil, water, crop, and livestock uptakes to human dermal and oral exposure.

---

[1] A Block Group (BG) is a subdivision of a Census Tract (CT), it is the smallest area listed in the Census Bureau's Master Area Reference File (MARF). BGs are replaced with roughly equivalent Enumeration Districts (EDs) in rural areas.

[2] As noted above, it was judged that particulate deposition was not important for manganese exposure from HiTEC®3000; therefore, the multipathway features of SCREAM were not needed for this work.

The SCREAM algorithm for estimating concentrations for distributed area sources such as motor vehicle traffic (gaussian plume treatments are used for fixed point, area, or volume sources) is a modified form of the Hanna-Gifford urban "box" model. The Hanna-Gifford model estimates a uniform urban concentration or a constant gradient along the wind as a function of wind speed, with a default coefficient recommended to represent the dispersion layer thickness (related to the height of the mixing lid) for large urban areas. In SCREAM the H-G concentration is scaled for each grid cell by the ratio of the cell emissions to the average cell emissions. Mean wind speed for each cell for each hour-of-the-day was computed from wind records, supplied by SCAQMD, for the closest of 33 meteorological stations.

Indoor concentrations in cars and buildings are computed with the Indoor Air Quality Model (IAQM [Hayes, 1991]) module, as a function of outdoor concentration, air exchange rates, air processing parameters, and pollutant-specific reaction rates (including deposition).

These features of SCREAM, and the availability of the data needed to apply the model to the SCAQMD emissions and population, allow the analysis of manganese dispersion and consequent human exposure for a large, metropolitan regional population. SCREAM may be used to address the exposures of people considering their locations, activities, and degree of sheltering appropriate to their group statistics, based on real data. Thus, results would define more accurate mean, or typical exposures and also give more realistic ranges of exposure from minimum to maximum and define the concentration levels to which each population group would be likely to be exposed.

It was decided to use this capability to address the refinement of EPA screening estimates of inhalation exposure to motor fuel related manganese. Deposition and associated dermal and oral exposures were not calculated.

SCREAM does not include activity data for garages because the time spent is much less than one hour. Because of the perceived high exposure in this micro-environment, separate, auxiliary calculations of exposure in this micro-environment were made. These calculations followed the

methods relied on in the ORD staff study, using, however, exposure times of 1.5 minutes on entering and 0.5 minutes leaving. Garage exposures were added to those from SCREAM.

Study Region

SCREAM modeling of exposures due to HiTEC°3000-related emissions was done using the SCAQMD as a study region.

Although the SCREAM model can be applied to any urban or rural area, regionally specific data for applying SCREAM to the SCAQMD had been supplied by South Coast agencies and was available for the present application. Thus, it would be desirable to model exposures to HiTEC°3000 exhaust products in the SCAQMD if the region were judged to be representative of the nation in terms of exposures to motor vehicle exhaust emissions. The results of an application to one metropolitan region cannot be simply extrapolated to the exposures expected for the entire U.S., but the region incorporates about 5 percent of the national population, and therefore the results should be significant in terms of the national population.

In the present case, several considerations suggest that exposures in the region might be greater than the average for the nation. Differences between the character of the SCAQMD and other population areas include the following:

- The physical size of the region is large, as is the population. Since the concentrations of vehicle exhaust increase with the scale of the urban region, and the emissions increase with total vehicle miles travelled (vmt), which in turn increase with the regional population, exposures in the SCAQMD should be at higher concentrations than in most other regions.

- The region is noted for dependence on automobile transportation; thus the vmt per person is higher than in many other areas and people spend more of their day in

vehicles and on roadways, thus producing higher than average exposure concentrations and exposure hours.

- The climate is moderate; thus homes are not as well sealed to drafts, may have windows open more, and may not need as much air conditioning (with its filtration of the air). The lower than average indoor sheltering of this region would again lead to an overestimate of the mean national exposure.

- The region has a very low mean wind speed. The average for all 33 SCAQMD stations, for all hours of the day, was computed to be about 2.5 m/s. This compares to a population-weighted average wind speed from national sites in the U.S. (Mara and Lee, 1978, cited in SAI, 1983) of 5.5 m/s. Since ambient concentrations increase with decreasing wind speed, the SCAQMD concentrations would be atypically high from this factor.

- The region has very low rainfall; thus precipitation scavenging of suspended particulates is minimized, and average ambient concentrations are maximized (i.e., the modeling analysis would come closer to actual expected ambient concentrations than in regions with substantial periods of precipitation.)

If results from the study of the SCAQMD show insignificant exposure, national exposure levels should be even less significant. Even if the SCAQMD is not the highest exposed area, the exposure for other population groups would not be likely to be enough larger to be of concern. For these reasons the SCAQMD was judged to be an appropriate study area for estimating HiTEC°3000-related manganese exposures.

DATA

The following paragraphs describe the data and data sources relied on to carry out the SCREAM modeling of the Los Angeles metropolitan region.

Meteorology

Meteorological data in the form of hourly wind and stability data for each of the SCAQMD's 33 wind measurement stations was supplied to Systems Applications, International by the SCAQMD. SAI processed the data with a computer code that produced the mean wind speed for each wind station for each hour-of-day.

Emissions

Manganese emissions were estimated by assuming that they were proportional to CO emissions. CO emissions were taken from a gridded emission inventory for the SCAQMD. The 1985 traffic data (VMT, speeds, etc.) was developed by the South Coast Association of Governments, the vehicle emissions and fleet aggregation by the California Air Resources Board, and the gridded aggregations for photochemical model input by the SCAQMD staff.

The mean CO emissions in grams/mile were extracted from the inventory; the mean Mn emission rate in grams/mile was taken from the average for all tests conducted by the EPA for all vehicle types and driving cycles. The Mn data indicated a mean emission of about 12 percent of the fuel Mn of 1/32 gram/gallon. The gridded Mn emissions were taken as $Mn(x,y) = CO(x,y)*[q(Mn)/q(CO)]$ for hour-of-day and day-of week. Since the q(Mn) was not determined for the same fleet and driving cycle as the q(CO), there is some error in the Mn emission pattern. This is thought to be less than the uncertainty of the gridded CO emissions.

Background Manganese Concentration

A constant, non-fuel additive related background concentration of 0.04 ug/m3 was assumed.

Indoor Modeling Parameters

Building stock data for each of four utility subdistricts, including characterization by building age and type (residence, commercial, office, school) and home weatherization and air conditioning were supplied by the California Energy Commission. Tightness of non-residence buildings was inferred from age relative to tightness affecting changes in the building code. A deposition rate for 2.5 micron particles was used.

Population

Residential location by US Census Block Group was extracted by SAI from 1980 MARF files obtained from the Census Bureau. Data on population by 56 cohorts and commute exchanges of cohort populations among 36 RSAs for each hour-of-day was provided by the South Coast Association of Governments (SCAG). After cohort exposures are determined, SCREAM aggregates the cohorts into 12 age-occupation groups for manageability of results. Daily activity patterns by hour-of-day for each of the cohorts was taken from files of national data prepared by the EPA for use in NEM modeling. The age-occupation groups include the following:

Managers and professionals
Sales workers
Clerical workers
Craftsmen and foremen
Machine operators and laborers
Farmers
Service and household workers

Adults working at home
Unemployed and retired
Children, age less than 5
Children, age 5 through 17
Students, age 18 or more

Micro-environments

Indoor modeling parameters were assembled for 11 micro-environments. These included the numbers of offices, schools, and homes and the fraction of these that are weatherized or air conditioned. Micro-environments include the following:

Non-weatherized office
Weatherized office
Non-weatherized school
Weatherized school
Non-weatherized home
Home, windows open
Home, air conditioning on
Inside vehicle
Outdoors, near road
Outdoors, not near road

Other parameters specified include indoor reactivity (in this case, indoor reactivity is primarily a measure of particulate deposition on indoor surfaces), make-up air filter efficiency, and recirculation air filter efficiency.

RESULTS

Results of the modeling are presented in the accompanying figures. The mean, incremental inhalation concentration was estimated as about 0.009 ug/m3 for exposures in the micro-environments addressed by SCREAM. The exposures of various age-occupation groups are presented in Figure 1 for SCREAM results only (i.e., without garage exposures or background), since only these addressed age-occupation data. Age-occupation exposures vary by over 50 percent, with the highest exposures to people who spend the most time outdoors or in unfiltered indoor atmospheres. The cumulative distribution of exposures (with non-motor vehicle background, but without garage exposures) presented in Figure 2 shows that the most exposed Census Block Groups receive about twice the mean exposure.

These results for Los Angeles may differ from results for other urban areas because of different building construction or use (LA windows are often open), different population or traffic densities, or different commute patterns, or for other reasons. These variations are not thought, however, to be sufficient to change the basic conclusions that the expected manganese exposures are small.

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Manganese Increment from Use in MVs

(SCREAM Modeled, by Activity Pattern)

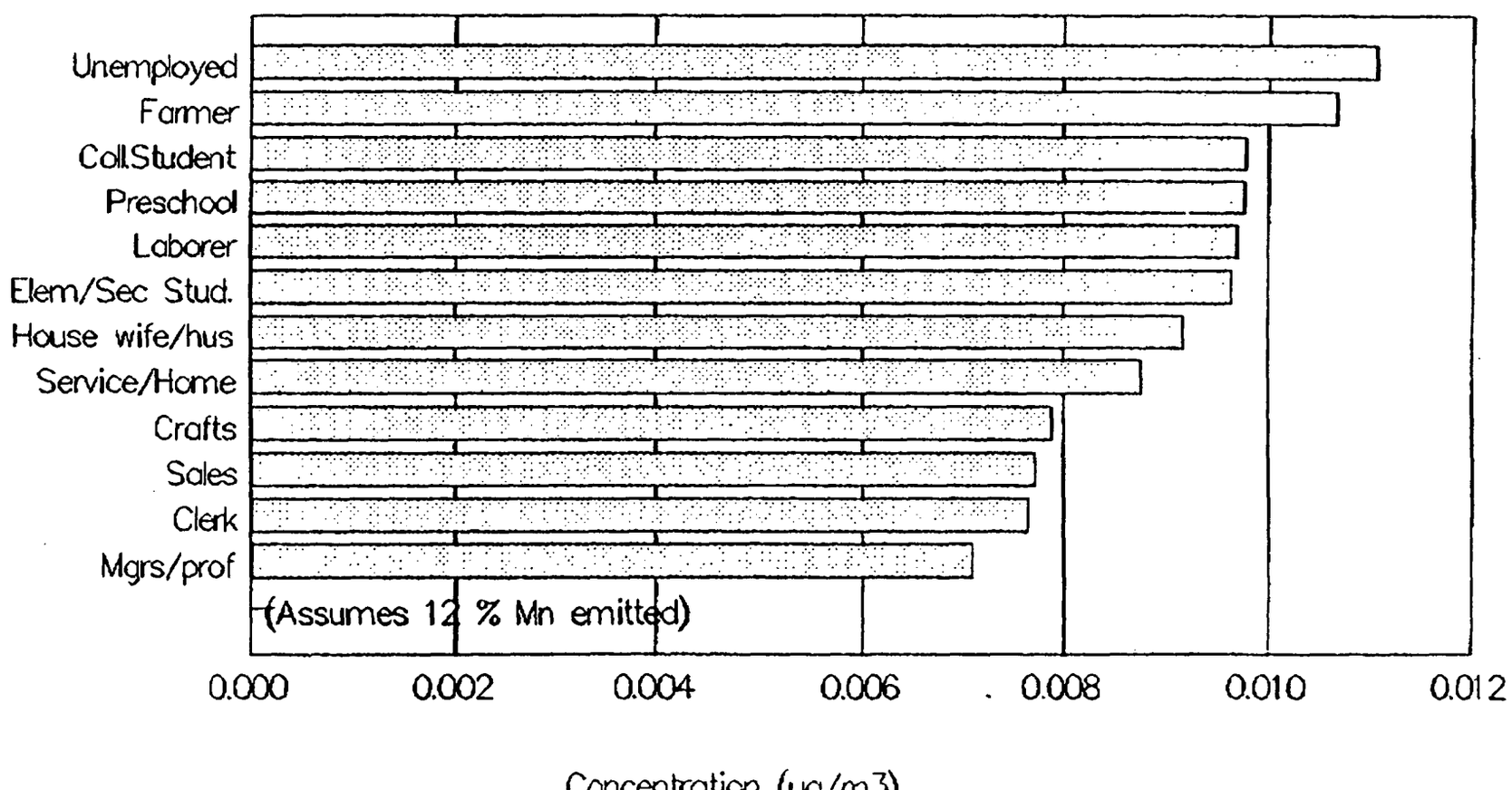

Figure 1.

CUMULATIVE POPULATION EXPOSURES

FROM SCREAM MODELING IN SCAQMD

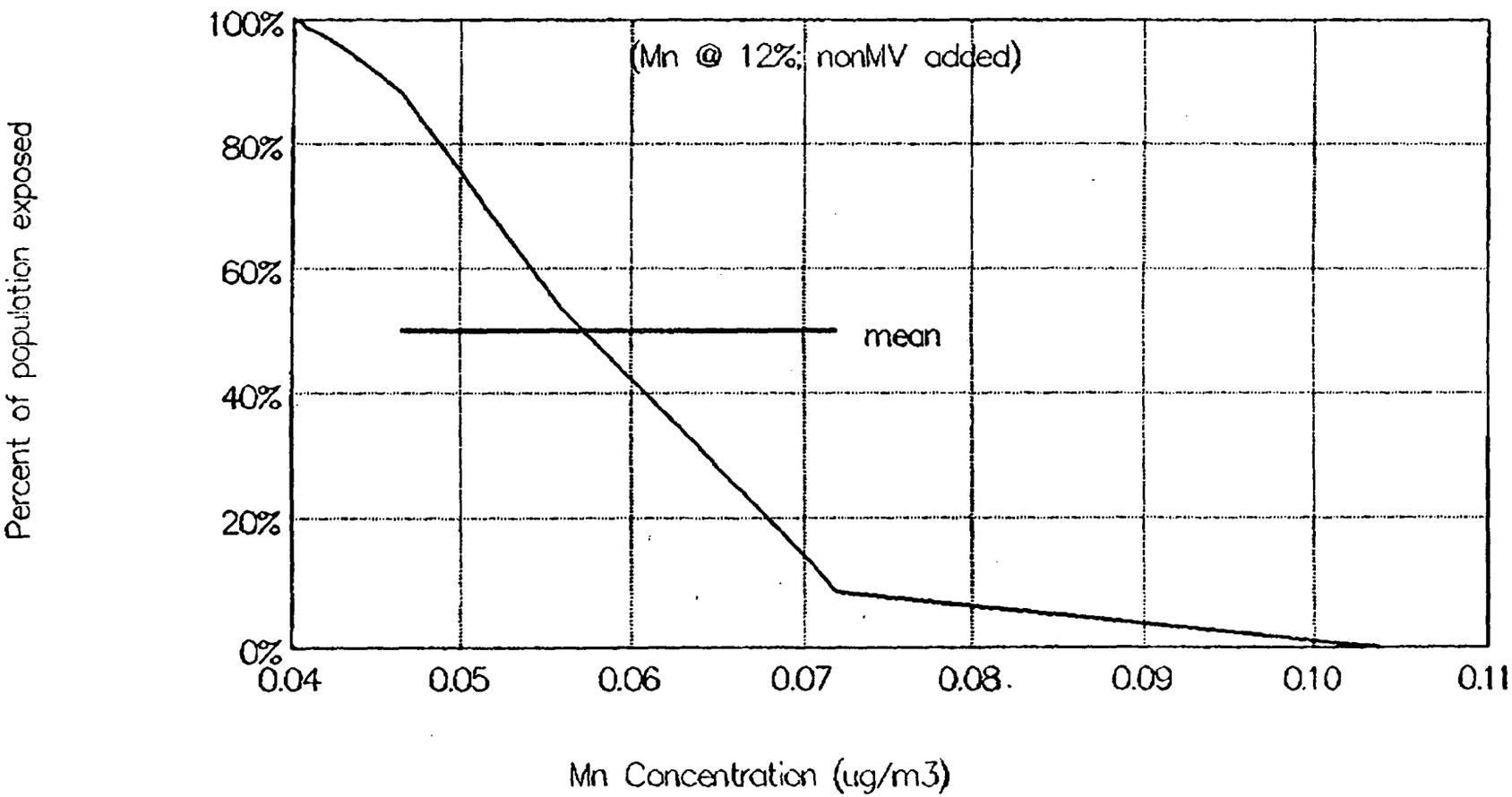

Figure 2.

ATTACHMENT 3

Use of Historical Metal Data to Model Manganese Exposures

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Ben F. Fort, Ph.D.
Ethyl Corporation
451 Florida Street
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Abstract

EPA's Office of Research and Development predicted manganese exposures from HiTEC 3000 (MMT) based upon modeling using carbon monoxide as a surrogate for manganese. Data is presented to show that it is inappropriate to use a gaseous substance as a surrogate for a particulate. Therefore, a model based upon traffic-related airborne lead was developed. The large database of historical lead-in-air measurements can be utilized to accurately predict manganese air levels resulting from use of MMT in unleaded gasoline. Calculations are based upon ambient lead levels reported in several cities by EPA and others at various times. Future airborne manganese levels are predicted from the ratio of lead used in gasoline to projected manganese use in gasoline.

Based upon very conservative assumptions in these calculations, levels of airborne manganese for most cities are predicted to average about 0.050 ug/m^3 if MMT is used at the maximum level requested in all gasoline. These levels include background manganese in air of 0.03 ug/m^3 from non-traffic-related sources. Levels in Los Angeles, because of the extremely heavy traffic patterns and unique geographic and atmospheric conditions, would be somewhat higher and could be taken as the worst case situation. The predicted values for airborne manganese in Los Angeles average about 0.07 ug/m^3. These predicted values are in very good agreement with airborne manganese levels measured in Toronto, Ontario, Canada, where MMT is used in gasoline up to levels approximately twice the level proposed for use by Ethyl in the U.S. This supports the validity of using lead-in-air data to predict future manganese-in-air levels.

The lead model was then utilized to predict average exposures of various population groups based on literature values for lead exposures in these populations. The predicted exposures to manganese are considerably below the proposed R_fC for manganese, even for Los Angeles cab drivers who presumably would have the highest exposure to traffic-related airborne manganese of any population group. Therefore, these calculations show that potential exposures of the general population to manganese from MMT use would be well within safe levels.

Rationale

In response to Ethyl's request for a waiver to use HiTEC 3000 Performance Additive (MMT) at a level of 0.03125 g Mn/gal, the EPA's Office of Research and Development (ORD) developed comments.(1) EPA proposed an Inhalation Reference Concentration (R_fC) for manganese of 0.4 ug/m^3 based upon a report of Roels et al.(2) This level is considerably below the recommended guideline by the World Health Organization (WHO) of 1.0 ug/m^3 as an annual average.(3) The WHO considers that this level incorporates a sufficient margin of safety to be protective of even the most sensitive population groups. The U.S. Occupational Safety and Health Agency (OSHA) has set a Permissible Exposure Limit for manganese fume (manganese oxide) of 1,000 ug/m^3 as an 8-hour Time Weighted Average.(4) In 1984, the EPA completed an extensive review of manganese-related health effects.(5) As a result, EPA concluded that manganese need not be regulated as a toxic air pollutant even though modeling suggested levels of 125 ug/m^3 for up to 8-hours could be achieved in some areas.(6)

The Agency for Toxic Substances and Disease Registry (ATSDR) recently issued a Toxicological Profile for Manganese in a Draft form.(7) Even though a draft, "It has been reviewed by scientists from ATSDR, the Center for Disease Control, the NTP and other federal agencies. It has also been reviewed by a panel of nongovernment peer reviewers..." The ATSDR derived a Minimal Risk Level (MRL) of 2 ug Mn/m^3 as being safe for long-term exposure. They say, "If a person is exposed to manganese at an amount below the MRL, it is not expected that harmful health effects will occur."

The setting of the R_fC for manganese at 0.4 ug/m^3, based on a study in which no dose-response was shown, is critical because of uncertainties in the models used by EPA to predict exposures from MMT use. The large standard deviations in the CO model discussed below led to the conclusion that significant numbers of people could be exposed above the R_fC. As noted in the ORD Document, "The resulting exposure estimates are viewed as order of magnitude estimates." Because of all the uncertainties in setting the R_fC and calculating potential exposures, the need for more refined modeling exists.

The ORD presented calculations of potential exposures to manganese in a number of microenvironments using carbon monoxide (CO) as a surrogate for manganese.(1) They estimated exposures of a "typical office worker" based on an estimated time spent in each microenvironment. Estimated exposures were calculated at various percentages of manganese emitted from the tailpipe. EPA assumed 100% of emitted manganese would remain airborne for some extended period. They also assumed that 100% of the inhaled manganese would be absorbed into the body.

The EPA admitted that there were large uncertainties in their approach. Ethyl feels there are a number of ways their estimates can be refined. The most fundamental error probably is the use of CO, a gas, as a surrogate for manganese, a particulate in air. There are basic differences in the behavior of airborne particulates versus gases as discussed below. In addition, there are many other sources of CO in microenvironments including water heaters, stoves, and charcoal grills.

Gases do not "settle out" and become deposited as do solids. Once released into the atmosphere, they remain until they are transformed chemically or undergo absorption/adsorption processes. There are several reports indicating that CO is not a good surrogate for traffic-related airborne lead except when sampled very close to heavy traffic. Lynam,[9] showed that the ratio of CO/Pb increased by a factor of 2 as the downwind distance from a busy expressway in Cincinnati increased from 20 feet to 640 feet. The ratio upwind was about 9 fold higher than 20 foot downwind levels. Huntzicker et al.[10] reported major differences in the CO to Pb ratio at various locations in the Los Angeles basin. Colucci et al.[11] reported a strong correlation between airborne lead and CO at various sampling sites in New York, Detroit and Los Angeles. However, the regression equations were site specific with intercepts ranging from -1.83 to 2.90 and slopes ranging from 0.39 to 1.42. In addition, there are many other sources of CO than traffic. These factors result in the large standard deviations in CO exposures noted in the ORD document

Another potential error made by the EPA is the assumption that indoor manganese levels would be the same as those outdoors. Indoor levels of airborne lead are considerably lower than outdoor levels. EPA states in the Lead Criteria Document "Overall, the data suggest indoor/outdoor ratios of 0.6-0.8 are typical for airborne lead in houses without air conditioning. Ratios in air conditioned houses are expected to be in the range of 0.3-0.5 (Yocum, 1982)."[8] Since traffic-related manganese aerosols are similar to traffic-related lead aerosols, they should behave in a like manner. Because most individuals spend the majority of their time indoors, personal exposure to manganese from MMT use should be lower than predicted by the ORD calculations.

Therefore, using another traffic-related airborne particulate as a surrogate for airborne manganese from the use of MMT in fuel should give a better estimate of potential exposures. Because of the vast amount of data reported in the literature on airborne lead in various microenvironments and because traffic-related lead is similar in many ways to traffic-related manganese, lead is an excellent surrogate. Ter Haar et al.[12] showed that manganese particulates emitted from automobiles using MMT were of about the same mass median aerodynamic diameter as lead particulates emitted from automobiles. Therefore, the behavior of manganese particulates in air should closely resemble that of lead particulates. In addition, the percentage of manganese used in gasoline that is emitted to the air is similar to the

percentage of lead emitted to the air.[12] Background levels of airborne lead are low and a large portion of lead emitted to the atmosphere in the U.S. was vehicular related before major reductions in lead antiknock usage occurred.[13] Other factors include changes in point source emissions and atmospheric conditions. These facts all suggest that lead could be a useful surrogate for manganese in modeling for potential increases in airborne manganese from MMT usage.

Ambient Levels

The calculations for predicting ambient manganese levels were based on the ratio of g Pb/gal of gasoline at the time the air lead levels were measured vs. the projected allowable level of manganese in gasoline if the waiver is granted (0.03125 g Mn/gal). The average concentration of lead in the gasoline pool has varied over the years for which air data are available from a high of 2.51 g Pb/gal to 0.49 g Pb/gal. The average concentration of lead in the total gasoline pool at the time measurements were taken was used in the calculations.

Simply multiplying the air lead concentration (less that amount not traffic-related) by the ratio of projected manganese concentration to lead concentration would give a reasonable estimate of the incremental increase in airborne manganese from MMT use. To project ambient levels, however, the background levels (non-traffic-related) levels of manganese need to be considered.

The background level of airborne lead was determined from regression analysis of EPA data on air lead concentrations versus lead-in-gasoline usage. By this method, a background level in urban areas of about 0.1 ug Pb/m^3 was calculated. This is confirmed by examining air lead measurements in urban areas as reported by EPA.

The EPA reported levels of manganese in urban areas in 1982 were about 0.033 ug/m^3.[6] Since MMT was used in leaded gasoline at that time, a background level of 0.03 ug Mn/m^3 was assumed. Therefore, to estimate future ambient levels of manganese, 0.1 ug/m^3 is subtracted from the measured air lead level and 0.03 ug/m^3 manganese is added as shown in the following equations.

Traffic-Related Mn in Air; Equation 1

$$MnA = (PbA-0.1) \times \frac{0.03125 \text{ g Mn/gal}}{\text{[Pb]/gal when PbA determined}}$$

Total Ambient Mn in Air; Equation 2

$$MnA = (PbA-0.1) \times \frac{0.03125 \text{ g Mn/gal}}{\text{[Pb]/gal when PbA determined}} + 0.03$$

Ambient air lead levels in urban areas have changed as gasoline lead usage has changed. However, predicted ambient manganese levels remain relatively constant. This supports our model as being valid. Table 1 shows results from air sampling in Los Angeles reported in two studies utilizing the same sampling stations.[14,15] Sampling was carried out from December 1961-November 1962 and December 1968-November 1969 in the two studies. Using the data reported and the formulas 1 and 2 shown, the estimated incremental increases in manganese air levels at these sites were calculated. Tables 2 and 3 show data from the same studies reported for Philadelphia and Cincinnati respectively. These two cities had lower air lead levels than Los Angeles. Therefore, the manganese-in-air projections were also lower. There was very good agreement in the predicted incremental increase and ambient levels of manganese in all three cities from year to year.

The projected incremental increase and ambient levels of manganese were also calculated from air lead data reported by EPA in the Lead Criteria Document for nine cities.[8] EPA reported the data as quarterly averages. The annual average for each city was estimated from the average of these quarterly averages. Data was only utilized when averages for two or more quarters were reported. Year-to-year variation of predicted ambient manganese levels had little variation even though there was about a 5-fold variation in lead concentrations over the time period in question. For instance, ambient levels were predicted to range from 0.043-0.058 for New York City using (Table 4). The average of the predicted values was 0.049. During the period in question, the lead concentration varied from 0.49-2.37 g/gal.

Table 5 shows the average predicted ambient levels of manganese for the 9 cities listed in the lead criteria document. The levels were relatively constant, around 0.05 ug/m^3, except for Los Angeles, California for which the predicted levels were slightly higher, about 0.070-0.075 ug/m^3. The next highest average is for "commercial sites" in Dallas/Ft. Worth. There are several point sources of lead which would lead to spurious results. If one considers the "all site" data, the average predicted level is about 0.05 ug/m^3, in line with the other cities.

We can test the validity of our model by comparing predicted values to real-life values. The Canadian experience gives us the opportunity to do this as MMT is allowed for use up to about twice the concentration proposed by Ethyl for use in the U.S. The Ontario Ministry of the Environment has an extensive air sampling network and reports on air levels of a number of substances including manganese.[16] Results from several sampling stations in the Toronto metropolitan area are shown in Table 6. As can be seen, the annual average values reported are in good agreement with predicted values from this model. The results from stations 31104 and 31120 could be taken as possible worst cases for traffic-related manganese for

Toronto (population over 2,000,000). Cities with point sources have much higher levels of airborne manganese. For instance, Hamilton, Ontario, which has several ferro-manganese steel producing facilities, has ambient manganese levels of about 0.16 ug/m^3. Rural areas with no point sources nearby, average from 0.01-0.02 ug/m^3.

Personal Exposure

Perhaps the most relevant data in the literature is in the report of Azar et al.[17] Actual exposures to airborne lead were measured by these researchers as shown in Table 7. In this study, exposures were measured for 30 cab drivers each in Los Angeles and Philadelphia, Los Angeles office workers and 30 non-occupationally exposed persons in each of Starke, Florida and Barksdale, Wisconsin. The Philadelphia cab drivers' exposures were sampled for 26 days, and the Los Angeles cab drivers' exposures were sampled for 21 days. All other measurements were carried out for 14 days. Note that the standard deviations of the average exposures are much smaller relative to levels found than those for CO measurements utilized in the ORD document. Use of this data eliminates the need to estimate times spent in various microenvironments and uncertainties associated with estimating levels of airborne manganese in these microenvironments. Assuming the data are normally distributed (which must have been done for CO exposures in the ORD document), we can calculate the 99 percentile for these exposures. This is done by basing our calculations on average lead exposures plus 3 times the standard deviations for those exposures. These data are also shown in Table 7 for the Los Angeles and Philadelphia subjects. Samples in the rural locations were impacted by non-traffic-related lead exposures as explained in the original article.

Exposures of Los Angeles cab drivers can perhaps be taken as the worst case situation for exposure to traffic-related lead and therefore give the highest predicted exposures to manganese. The data predict average exposures of 0.109 ug Mn/m^3 for these subjects. Assuming the average person inhales 20 m^3/day, the predicted total 24-hour exposure to airborne manganese would be 2.18 ug Mn/day. These levels are significantly below levels predicted by the ORD model for "typical office workers" of 3.4 ug/day. The calculations predict inhalation exposures of 1.38 ug/day for office workers in Los Angeles. Predicted exposures in other cities would be lower because ambient levels of lead were lower. The 99th percentile of exposures based on the Azar et al. data was calculated by using the mean exposure plus three times the standard deviation as the airborne lead level. Even the 99 percentile exposure of the worst-case situation (Los Angeles cab drivers) was below the levels predicted for the "typical office worker" in the ORD calculations and well below the proposed R_fC.

Conclusions

Using lead as a surrogate to predict potential ambient levels of manganese with MMT usage gives reasonable values when compared to data from Canada. The large amount of historical lead data provides a very good source of information for estimating future manganese airborne levels and numerous uncertainties about future airborne concentrations of manganese. The model predicts exposures to airborne manganese at significantly lower levels than those derived by the EPA's Office of Research and Development. MMT usage at the level requested by Ethyl would result in manganese exposures well below the R_fD for the general population according to calculations based on literature values for personal exposures to lead.

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TABLE 1

Air Lead Levels - Los Angeles[14,15]

Year Sampled	Site Description	Measured Lead in Air (ug/m^3)	Incremental Increase in Manganese in Air from MMT Use (ug/m^3)	Total Predicted Manganese-in-Air Background + Increment (ug/m^3)
1961-2	Downtown	2.49	0.037	0.067
1968-9	Same as above	4.03	0.050	0.080
1961-2	Commercial 5' high	2.63	0.039	0.069
1968-9	1/4 mile north of above	4.23	0.053	0.083
1961-2	Rural Arcadia	2.61	0.039	0.069
1968-9	Same as above	3.46	0.043	0.073
1961-2	Residential 10'	2.27	0.034	0.064
1968-9	Same as above	3.72	0.047	0.077
1961-2	Residential	2.04	0.031	0.061
1968-9	Same as above	3.06	0.038	0.068
1961-2	Residential UCLA	1.49	0.022	0.052
1968-9	Same as above	2.36	0.030	0.060
1961-2	Industrial	2.17	0.032	0.062
1968-9	Same as above	3.39	0.042	0.072
1961-2	Downtown	2.80	0.042	0.072
1968-9	Same as above	4.55	0.057	0.087

TABLE 2

Air Lead Levels - Philadelphia[14,15]

ar pled	Site Description	Measured Lead in Air (ug/m^3)	Incremental Increase in Manganese in Air from MMT Use (ug/m^3)	Total Predicted Manganese-in-Air Background + Increment (ug/m^3)
1-2	U.S. Naval Hospital	1.39	0.021	0.051
8-9	Same as above	1.89	0.024	0.054
1-2	Commercial	1.75	0.026	0.056
8-9	Same as above	1.74	0.022	0.052
1-2	Commercial	3.27	0.049	0.079
8-9	Across street	3.75	0.047	0.077
1-2	Industrial	2.13	0.032	0.062
8-9	Industrial	2.18	0.027	0.057
1-2	Residential	1.10	0.017	0.047
8-9	Residential	1.39	0.017	0.047
1-2	Rural	0.87	0.013	0.043
8-9	Rural	1.09	0.014	0.044
1-2	Rural	0.86	0.013	0.043
8-9	Rural	1.08	0.014	0.044

TABLE 3

Air Lead Levels - Philadelphia[14,15]

Year Sampled	Site Description	Measured Lead in Air (ug/m^3)	Incremental Increase in Manganese in Air from MMT Use (ug/m^3)	Total Predicted Manganese-in-Air Background + Increment (ug/m^3)
1961-2	Commercial	1.70	0.026	0.056
1968-9	Commercial	1.92	0.024	0.054
1961-2	Residential	1.09	0.016	0.046
1968-9	Residential	1.45	0.018	0.048
1961-2	Industrial	1.70	0.026	0.056
1968-9	Industrial	2.13	0.027	0.057
1961-2	Rural	0.87	0.013	0.043
1968-9	Rural	0.85	0.011	0.041

TABLE 4

Predicted Ambient Manganese-in-Air Levels for New York City

Year	Pb Conc. (g/Gal)	PbA Measured (ug/Cu Meter)	Incremental Incentive in Manganese in Air from MMT Usage (ug/Cu Meter)	Predicted Ambient Manganese-in-Air Background + Increment (ug/Cu Meter)
1970	2.37	1.5	0.018	0.048
1971	2.20	1.7	0.023	0.053
1972	2.05	1.1	0.015	0.045
1973	1.93	1.0	0.015	0.045
1974	1.74	0.85	0.013	0.043
1975	1.59	0.93	0.016	0.046
1978	1.32	1.3	0.028	0.058
1979	1.16	1.0	0.024	0.054
1982	0.62	0.53	0.022	0.052
1983	0.49	0.35	0.016	0.046
Minimum	0.49	0.35	0.013	0.043
Maximum	2.37	1.7	0.028	0.058
Average	1.55	1.03	0.019	0.049

TABLE 5

Summary of Predicted Manganese in Air Levels
Average of Levels Based on Lead Data Presented
In EPA Lead Criteria Document

City	Commercial Sites	All Sites
Boston	0.048	
New York	0.048	
Philadelphia	0.055	0.047
Washington	0.052	
Detroit	0.046	
Chicago	0.046	0.044
Houston	0.053	0.049
Dallas/Ft. Worth	0.059	0.051
Los Angeles	0.073	0.070

TABLE 6

Airborne Manganese - Toronto and Environs[15]

Sampling Station #	Location	Description	ug Mn/m^3 1985	1986	1987	1988
31104	26 Breadalbane	Downtown	0.039	0.031	0.050	0.046
31120	Perth/Ruskin (Junction Triangle)	Expressway	0.041	0.026	0.044	0.039
33003	Lawrence/Kennedy Scarboro	N.R.	0.047	0.035	0.051	N.R.
34002	SC Centre, 770 Don Mills Road, North York	Commercial	0.036	0.025	0.045	N.R.
35003	Elmcrest Road, (Centennial Park) Etobicoke	N.R.	0.042	0.040	0.055	N.R.

N.R. = Not Reported

TABLE 7

Personal Exposures Predicted from Lead Model[17]

City/Occupation	Average Airborne Lead Exposure (ug Pb/m^3)	Predicted Mean Airborne Manganese Exposure (ug Mn/m^3)	Predicted Average Airborne Manganese Exposure 99 Percentile (ug Mn/m^3)
Los Angeles Cab Drivers	6.10 ± 0.81	0.109	0.141
Los Angeles Office Workers	3.06 ± 0.75	0.069	0.099
Philadelphia Cab Drivers	2.62 ± 0.42	0.063	0.080
Barksdale, Wisconsin	1.01 ± 1.43	0.042	-
Starke, Florida	0.81 ± 0.82	0.039	-

ATTACHMENT 4

TECHNICAL NOTE

ESTIMATING EXPOSURES TO MANGANESE FROM THE USE OF HiTEC 3000 IN UNLEADED GASOLINE

April 1991

Prepared for

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INTRODUCTION

The purpose of this technical note is twofold. First, we review EPA's estimate of distributional (extreme) exposures to manganese that may result from using HiTEC 3000 in unleaded gasoline.* Second, we identify an alternative means for determining distributional exposures and apply this alternative to EPA's estimate of average manganese exposures.

DISCUSSION

The initial focus of our analysis is to review the EPA/ORD estimate of distributional (extreme) exposures. Table 1 is reproduced from the EPA/ORD assessment and shows a distribution of exposures as a function of percent of input manganese emitted. EPA/ORD obtained its distributional estimate of exposures by multiplying average manganese exposures by a factor determined from the distribution of exposures to CO (Mage et al. 1989).

The EPA/ORD algorithm for estimating exposures consists of three components: (1) a fixed background concentration (0.04 $\mu g/m^3$); (2) an incremental addition to background concentration as a result of using MMT in unleaded gasoline; and (3) an elevated concentration due to microenvironmental activity. In estimating distributional exposures, EPA/ORD multiplied the sum of incremental background concentration and microenvironment concentrations times the CO-derived distributional factor. We believe that the incremental background concentration should <u>not</u> be multiplied by the CO-derived factor. That is, the EPA/ORD methodology is based on a uniform increase in background concentration as a function of

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* "Comments on the Use of Methylcyclopentadienyl Manganese Tricarbonyl in Unleaded Gasoline", Office of Research and Development, Environmental Protection Agency, Washington, D.C., November 1, 1990.

percent of input manganese emitted, and therefore should not be increased by a multiplying factor. In other words, as a true background component, there can be no microenvironment or activity pattern that gives rise to concentrations in excess of the background increment. Accordingly, we repeat the EPA/ORD distributional calculations but do not multiply the background increment times the CO-derived distributional factor. These results are presented in Table 2. The difference in results is significant for extreme exposures (i.e., 99.4 percentile) and for high percentages of manganese emitted (i.e., greater than 30 percent).

The next step in our analysis is to identify another set of data on which to estimate distributional exposures. Azar, et al. (1972) conducted a study of exposure to airborne lead.[=] The Azar study is particularly relevant to this analysis because lead is the only other widely used metallic fuel additive and, at the time of the study, lead use as a fuel additive was at its peak. Moreover, unlike CO, lead emissions from motor vehicles are particles and should disperse in ambient air more like manganese than does CO.

Azar, et al. sampled 30 male subjects in each of five locations: Los Angeles office workers, Los Angeles cab drivers, Philadelphia cab drivers, and Dupont employees in Starke, Florida and in Barksdale, Wisconsin. Samples were collected over a period of 2 to 4 weeks. Dual samplers were used to differentiate between "on-duty" and "off-duty" exposures. Results reported by Azar, et al. are for individual exposures and are averaged over the 2-4 week sampling period. Our approach for estimating distributional exposures using data from Azar, et al. is described below.

[=] A copy of the Azar study is attached to this technical note.

The first step is to identify the sample group within the Azar, et al. study that most closely resembles the group analyzed by EPA/ORD. The logical choice is the Los Angeles office workers because EPA/ORD based its analysis on an office worker who is assumed to have a home garage, commutes to work in a downtown office, and parks his car in a parking garage relatively near to his office. Moreover, we note that the most relevant data are those obtained for "on-duty" exposure. On-duty concentrations are appropriate because we are adjusting exposures that occur from time spent in certain microenvironments (e.g., commuting, parking garages, etc.). Other exposures (e.g., at home) are accounted for by fixed background and incremental background contributions. The next step is to identify data indicative of extreme exposures. The maximum exposed person is given by the highest "on-duty" concentration of a Los Angeles cab driver. The minimum exposed person is given by the lowest "on-duty" concentration of a Dupont employee in Barksdale, Wisconsin. Using these maximum and minimum concentrations in conjunction with the average, "on-duty" Los Angeles office worker concentration, we develop the following factors to estimate maximum and minimum exposures to manganese. For maximum exposure, we divide the maximum, on-duty Los Angeles cab driver concentration (11.29 $\mu g/m^3$) by the average Los Angeles office worker on-duty concentration (3.05 $\mu g/m^3$) to obtain a factor equal to 3.70. For minimum exposure, we divide the minimum, on-duty Barksdale employee concentration (0.14 $\mu g/m^3$) by the average Los Angeles office worker on-duty concentration (3.05 $\mu g/m^3$) to obtain a factor equal to 0.046.

We estimate maximum and minimum exposures by multiplying these factors times EPA's estimate of average (50 percentile) exposures (see Table 1). Results are shown in Table 3. Our computations include exposure due to an assumed incremental increase in background concentration but, as discussed

earlier, we do not multiply the background increase times either of the distributional factors. Since 150 individuals were sampled by Azar, et al., maximum and minimum estimates approximate exposures at the 0.7 and 99.3 percentiles.

SUMMARY

Distributional (extreme) exposure estimates based on data from Azar, et al. are significantly different from those obtained by EPA/ORD, which are based on CO-derived factors. The CO data used by EPA/ORD exhibit a large variation in CO concentration (e.g., the 99.4 percentile is 9.5 times the mean CO concentration). Given the many and diverse sources of CO in a typical urban environment, the above result is not surprising. Furthermore, the CO concentrations are based on 8-hour averages, which are inherently more variable than are corresponding 24-hour averages. For reasons previously stated in this technical note, we believe the lead exposure data from Azar, et al. are a better predictor of extreme manganese exposures than are factors derived from CO data. Using the lead exposure data to predict manganese exposure from the use of HiTEC 3000 in unleaded gasoline show that maximum exposures, assuming 30 percent of input manganese is emitted, are less than 3 μg/day.

TABLE 1. EPA EXPOSURE ESTIMATES (μg/day)

Percent Mn Emitted	Potentially Exposed Population (10^6)					
	160 (85%)	140 (75%)	95 (50%)	50 (25%)	20 (10%)	1 (0.6%)
Current Background	.8	.8	.8	.8	.8	.8
0.4%	.8	.8	.8	.9	.9	1
10%	.9	.9	1	1	2	3
20%	1	1	1	2	2	6
30%	1	1	2	2	3	8
40%	1	1	2	3	4	10
60%	1	2	2	4	5	20
100%	2	2	3	5	8	30

SOURCE: EPA/ORD Risk Assessment, October 1990.

TABLE 2. REVISED[1] EPA EXPOSURE ESTIMATES (μg/day)

Percent Mn Emitted	Potentially Exposed Population (10^6)					
	160 (85%)	140 (75%)	95 (50%)	50 (25%)	20 (10%)	1 (0.6%)
0.4%	.81	.81	.81	.81	.82	.86
10%	.95	.98	1.06	1.18	1.35	2.44
20%	1.10	1.16	1.32	1.55	1.89	4.08
30%	1.25	1.34	1.58	1.92	2.43	5.70
40%	1.39	1.52	1.85	2.30	2.98	7.34
60%	1.69	1.89	2.37	3.05	4.07	10.6
100%	2.29	2.61	3.42	4.55	6.25	17.2

[1] Exposure due to incremental background contribution is only a function of percent Mn emitted. Ratios obtained from CO exposure data are only applied to microenvironment concentrations.

TABLE 3. RESULTS: ESTIMATED EXPOSURES (μg/day)

Percent Mn Emitted	Percent Exposed		
	Minimum	50%	Maximum
0.4	0.80	0.81	0.83
10	0.91	1.06	1.50
20	1.02	1.32	2.20
30	1.12	1.58	2.89
40	1.23	1.85	3.59
60	1.45	2.37	4.99
100	1.87	3.45	7.79

ON THE LACK OF RELATIONSHIP BETWEEN MANGANESE EXPOSURE AND IDIOPATHIC PARKINSONISM

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ATTACHMENT

(Azar, et al. Study)

3406

An Epidemiologic Approach to Community Air Lead Exposure Using Personal Air Samplers

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Abstract

Accurate information on the relationship between blood lead and air lead is essential to any consideration of the possible effect of air lead on the body burden. Past studies of occupationally exposed workers have established that such a relationship exists at high levels of air lead exposure. No such information has been available for subjects exposed to the low air lead levels representative of present-day community exposure.

Past studies in this area have suffered from inadequate information on actual lead exposure at the air lead levels of concern. Researchers have had to rely on air lead data obtained from stationary sampling stations. Because wide variations can exist between locations within a city such information could not be assumed to represent the exposure of any individual subject. At best they can be considered only approximations of actual exposures.

The National Research Council recognized the deficiencies of past studies in their report "Airborne Lead in Perspective" and recommended that "more precise studies are needed of the relation between atmospheric lead in the urban environment and the concentration of lead in the blood, perhaps by the use of personal monitors".

This paper describes the study which was undertaken to evaluate the effect of air lead exposure as measured with personal air sampling devices on indices of lead absorption such as blood lead, urine lead, DALA and ALAD activity. The air lead exposure of thirty male subjects in each of five locations (total 150) in the United States, was measured with personal air samplers for twenty-four hours a day for two to four weeks. During this period of time, blood samples were obtained for blood lead analyses and ALA-dehydrase activity. Urine samples were obtained for urine lead analysis, DALA excretion and osmolality and creatinine determinations. The five sites were selected to represent a wide range of air lead exposures. Taxicab drivers were studied in Philadelphia and Los Angeles. Participants at the other three locations were Du Pont employees who represented non-occupationally exposed groups.

Air lead exposures ranged from a low of 0.22 $\mu g/m^3$ at Strake, Florida, to a high of 9.12 $\mu g/m^3$ for a Los Angeles cab driver. It is significant that despite air lead exposures approaching 10 $\mu g/m^3$ only one individual had abnormal blood and urine responses and these could be attributed to sources other than air lead exposure.

A rigorous statistical analysis of the data showed that there was no significant correlation between air and blood lead at any of the five sites, indicating either (1) that there is in fact no correlation between air lead and blood lead, or (2) thirty subjects is too

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few to demonstrate significance, or (3) the range of data is too narrow to show significance, or (4) variables other than air lead (lead ingested from food and drink) are overwhelming any effect which air lead might have on blood lead. An analysis of the data for 149 of the subjects using a multiple regression technique indicated that variables other than air lead were affecting blood lead. This analysis showed that the model which gave the best fit to the data was not a single line but a series of lines having similar slopes but different intercepts. The different intercepts indicate the effect of variables other than air lead. The effect of air lead on blood lead was less than would have been predicted from the Goldsmith-Hexter correlation and considerably less than indicated by the theoretical calculations of the Environmental Protection Agency.

Introduction

The purpose of the present experiment was to determine whether there is any relationship between exposure to levels of inorganic lead found in the community atmosphere and indices of lead absorption such as blood lead, urine lead, δ-aminolevulinic acid dehydrase (ALAD) and δ-aminolevulinic acid (DALA).

Williams *et al.* (1), using personal air sampling devices for measuring lead in air have shown that industrial air lead exposures of eight hours per day to 150 μg Pb/m³ resulted in a blood Pb of 60 μg/100 gm, a urine Pb of 118 μg/liter and a urine DALA level of 1.4 mg/100 ml urine. Marked differences were found in the air lead exposure of workers doing the same task, pointing out the fallacy of air lead measurements obtained from a stationary air sampling device.

There is little controversy over the fact that there is a correlation between the high industrial air lead exposures and indices of lead absorption; however, there is considerable debate as to whether such a relationship exists at the lower concentrations of air lead (< 10 μg/m³) found in the community atmosphere.

Goldsmith and Hexter (2) using data obtained from the U. S. Public Health Service survey of Cincinnati, Philadelphia and Los Angeles concluded that there was a relationship between the logarithm of estimated air lead exposure and the logarithm of blood lead concentration. A later document (40) described the statistical method used to demonstrate that this relationship was not valid at air lead levels below 2 μg/m³. The validity of such a relationship has been challenged by Stopps (3) on the basis that the air lead exposures were estimated; the blood lead measurements were not necessarily done at the same time and place as the air lead determinations; and that the data had not been properly analyzed statistically to determine if the data from the different groups of subjects could be combined. More recently, the statistical method used in defining the 2 μg/m³ limit has also been challenged by Enterline (4) and McCaughran (5).

Preliminary analysis of a more recent investigation by Tepper (6) has failed to confirm the relationship described by Goldsmith and Hexter. The study by Tepper, commonly referred to as the Seven City Study, consisted of obtaining blood and fecal lead determinations on large groups of housewives living within a one mile radius of a stationary air lead sampling device.

The National Research Council (7, p. 325) has recommended that "more precise studies are needed of the relation between atmospheric lead exposure in the urban environment and the concentration of lead in the blood, perhaps by the use of personal monitors."
The study reported herein, was undertaken to obtain additional data on any potential relationship between air lead exposure as measured with personal air sampling devices and indices of lead absorption such as blood Pb, urine Pb, DALA and ALAD activity.

Methods

General Procedure:

The air lead exposure of thirty male subjects in each of five locations total 150) in the United States, was measured with personal air samplers for twenty-four hours a day for two to four weeks. During this period of time, blood samples were obtained for blood lead analyses and ALA-dehydrase activity. Urine samples were obtained for urine lead analysis, DALA excretion and osmolality and creatinine determinations.

Site Selection:

The demographic characteristics of the study are shown in Table 1. The five sites were selected to represent a wide range of air lead exposures. Taxicab drivers were studied in Philadelphia, Pennsylvania and Los Angeles, California. The participants at Starke, Florida, Barksdale, Wisconsin and Los Angeles were employees of E. I. Du Pont de Nemours & Company. The Du Pont employees are representative of non-occupationally exposed groups.

Subject Selection:

Participation in the study was limited to male day shift workers. In the taxicab studies only drivers from a downtown station were included. The average age of the subjects taking part in the study is shown in Table 1. Also included in Table 1 is the average number of years that participants drove taxicabs or worked at the plant site being studied. Each subject filled out a smoking questionnaire. The data of primary importance here were the subjects age, number of years smoking, and the amount of smoking.

Air Sampling:

The air lead exposure of each individual was monitored by means of personal air samplers. The personal air samplers used were: Casella Model "B" Personal Size Selection Gravimetric Dust Sampler manufactured by C. F. Casella and Company, Ltd., London, England, and the MSA "Gravimetric" Dust Sampling Pump manufactured by Mine Safety Appliance Co., Pittsburgh,

Table 1 Site characteristics

Site	No. Subjects	Date	No. Days	Age	Years on Job
Philadelphia, Pa. Cab Drivers	30	5/4-5/29/70	26	49.6 ± 8.0	17.7 ± 7.1
Starke, Fla.	30	6/18-7/1/70	14	49.1 ± 6.9	18.3 ± 4.8
Barksdale, Wisc.	30	7/29-8/12/70	14	51.3 ± 10.7	19.1 ± 9.6
Los Angeles, Calif. Cab Drivers	30	10/23-11/5 11/12-11/19/70	21	48.4 ± 9.9	16.0 ± 7.8
Los Angeles, Calif. Office Workers	30	2/4-2/18/71	14	44.2 ± 14.3	16.7 ± 11.3

Pa. The Casella unit had a 5.95 CFH (cubic feet per hour) flow rate and the MSA unit had a flow rate of 5.25 CFH. At some locations, a MSA cyclone device was used to separate out particles larger than 10 microns in diameter. It is generally agreed that particles larger than 10 microns are non-respirable. The particulate matter was collected on 0.8 micropore size 37 millimeter diameter filter paper purchased from the Millipore Corporation (Cat. No. MAWP037A0).

During the Philadelphia and Los Angeles taxicab studies, two MSA units were mounted under the dash of the cab and connected by plastic tubing to two filter heads mounted on the steering column. One of the filter heads was the cyclone device used to separate out non-respirable particles; and thus represented the respirable air lead exposure. The other filter head did not have the cyclone device; thereby, giving the total air lead exposure. Each two-unit set had an electrical timer and was wired to the hot side of the ignition system which allowed them to operate continuously, once their switch was turned on prior to the driver leaving the garage.

The taxicab driver's off duty air exposure was monitored with the battery operated Casella units. These units did not have a cyclone device and had a built-in timer which indicated the number of minutes the sampler was in use. The units were adapted so that they could be powered off of the cigarette lighter of the subject's personal automobile or off of their home power supply. The subjects were instructed to wear the air sampling unit when out-of-doors, with the filter head as close to their breathing zone as possible. A clip on the filter head permitted them to attach it to the lapel of their shirt or coat. When indoors, they were told that they did not have to wear the unit; however, it was to be kept on the same floor of the building that they were on, and located at a level near their breathing zone — for example, on top of a television, night table, or dresser, etc. The participants at the Du Pont locations wore the MSA personal air samplers during working hours. With the exception of Starke, Florida, the units worn at work did not have the cyclone device. The Starke location had some open mining going on which at times resulted in a rather dusty environment. Because of this, the subjects at Starke wore the MSA Cyclone devices at work. At all the locations, the subjects wore the casella unit while

Table 2 Summary of measurements made

Site	Respirable Pb	Total Pb	Urine[a] A.M.	P.M.	Blood[b]
Philadelphia, Pa. Cab Drivers	x	x	26	–	8[c]
Starke, Fla.	x	x	14	–	2
Barksdale, Wisc.	–	x	14	–	2
Los Angeles, Calif. Cab Drivers	x	x	21	21	6
Los Angeles, Calif. Office Workers	–	x	15	14	4

(a) – Each sample analyzed for lead, DALA, osmolality and creatinine.
(b) – Each sample analyzed for lead and ALA-Dehydrase.
(c) – Only seven samples analyzed for ALA-Dehydrase.

off duty and were issued the same instructions as those given the taxicab drivers. A summary of the air lead measurements made is shown in Table 2.

In the Los Angeles and Philadelphia studies, the filters were changed daily except for days off, and the airflow calculated. Due to the low air lead exposures at Starke and Barksdale, the filters were changed less frequently to permit more measurable quantities of lead to accumultae on the filters.

Air Lead Analysis:

The lead content of millipore filters was determined by a procedure involving acid digestion of the filter to solubilize the deposit and the filter. Then the lead is extracted from the diluted acidic solution into 5 ml of an organic solvent (methyl isobutyl ketone) using potassium iodide and Aliquot 336 (trioctyl methyl ammonium chloride) as complexing agents for lead. The amount of lead present in the organic solvent is determined with Perkin Elmer Model 403 Atomic Absorption Spectrophotometer at the absorption line of 2833 Angstroms. The accuracy of the method was ± 5 per cent or ± 0.1 μg Pb, whichever was larger.

Blood Measurements:

Blood and urine samples were obtained from each subject. Two blood samples a week were obtained during the two taxicab studies, and the Los Angeles office workers study. During these studies, one sample was drawn early in the week and the other towards the end of the week. At Starke and Barksdale, one blood specimen was taken at the beginning of the study, and the other at the end of the study period. The venipunctures were carried out when the subjects reported to work. Urine specimens were collected daily from each subject at the beginning of the work shift. On days off, the subjects collected their second voided specimen. In both of the Los Angeles studies, urine samples were obtained at the beginning of the shift (A. M.) and at the end of the shift (P. M.). The number of blood and urine specimens at each location are summarized in Table 2.

The blood specimens were collected from the antecubital vein in 10 ml B-D Vacutainer tubes containing 143 USP Units Sodium Heparin and certified to contain less than 0.05 micrograms lead. Each blood specimen was analyzed for lead and delta-aminolevulinic acid dehydrase (ALAD). During the Los Angeles Cab study, only, the subjects blood level of carboxyhemoglobin was also determined.

The blood was analyzed for lead by ashing 2.0 grams with 100 ± 10 mg MgO at 425° C to 450° C for 16 hours (8). The ash was dissolved in 2 ml of HCl (1 : 1) and diluted to 15.0 ml with H_2O. The concentration of lead in this solution was determined by anodic stripping voltammetry, utilizing a mercury on graphite as the working electrode (9, 10). All blood samples were analyzed for lead in duplicate. The standard deviation for each day's sampling (approximately 30 samples) over a seven month period was calculated. The eighteen standard deviations thus obtained ranged from 1.9 to 5.3 μg Pb/100 g with a pooled value of 3.8 μg/100 g.

ALA-Dehydrase was determined by the method of Bonsignore, *et al.* (11) and carboxyhemoglobin by the method of Amenta (12).

Urine Measurements:

The urine specimens were collected in nitric acid-washed glass containers and refrigerated until the determination of

δ-aminolevulinic acid (DALA) was completed (within 72 hours). Each urine sample was analyzed for lead, DALA, osmolality, and creatinine.

DALA was measured by the DAVIS [13] method using kits prepared by Bio-Rad Laboratories, Richmond, California. Each kit is supplied with a set of piggyback columns packed with ion exchange resin. All kits purchased prior to the Los Angeles Taxicab Study contained the resin in a dry form; however, those purchased for both Los Angeles studies arrived with the resin as a suspension in water which had to be drained prior to analyses. A comparison of the two methods (wet and dry) was made using urine samples from the thirty subjects in the Los Angeles Taxicab Study. Statistical analyses of the data showed that DALA (dry method) = 0.09 + 0.983 DALA (wet method). Since 0.983 (95% Confidence Limits = ± 0.178) is not significantly different from one, it was concluded that the wet method results averaged 0.09 mg/100 ml (95% Confidence Limits = ± 0.01) lower than the dry method. Thus all DALA results reported for the two Los Angeles studies were increased by 0.09.

Urine creatinine was analyzed by a modification of the procedure of FOLIN and WU [14] and osmolality was determined using a Fiske Osmometer.

Urine lead was measured by extraction/concentration of lead into an organic phase followed by determination of lead by atomic absorption [15]. The urine was made 1.1 M in HCl and 0.35 M in KI. Forty-four ml of the resulting solution was then extracted once with methyl isobutyl ketone (5.0 ml) containing 1% trioctyl methyl ammonium chloride ("Aliquot" 336, General Mills Co.). The organic phase was aspirated into a hydrogen/air flame and the atomic absorption measured at the 283.3 n m lead line. A techtron AA-4 atomic absorption spectrophotometer was used with a 10-cm single slot burner (AB-41). The H_2 and air flows were selected to give maximum signal to noise ratio. Likewise, the distance above the burner at which the light beam was centered was selected. The instrument was calibrated by running three standards with each batch of 30 samples. The standards consisted of approximately 4 μg Pb in 40 ml of distilled water replacing the urine. The standard deviation of the analysis was determined by running 80 samples, representing 40 duplicates during 21 working days by two technicians. The samples were randomized so that duplicates were usually run on different days. The standard deviation was 5.7 μg Pb/l over the range of 20 to 120 μg/l.

Statistical Analyses:

The average exposure, urine, and blood responses were computed for each subject in the study. All statistical analyses were based on these subject averages. The site averages for the blood and urine data were subjected to an analysis of variance to determine whether there were any significant differences between the average urine and blood responses of the five sites. The relationship between air lead and the blood and urine responses were evaluated using regression techniques. The homogeneity of the slopes were checked by multiple regression techniques. Analyses of the data in both natural physical units and logarithmic units (base 10 logarithms of the natural physical units) were carried out. The logarithmic relationship gave the best fit to the data; therefore, all conclusions were based on the logarithmic analyses.

Results

Air Lead Exposures:

The air lead exposure was calculated by combining the work exposure (On Duty) with the home exposure (Off Duty) on a timeweighted basis. When a cyclone device was used, the data are referred to as Respirable and when it was not used, Total. Unless stated, the exposures reported in this report are the average time-weighted exposure to total Pb.

The exposures ranged from a low of 0.22 $\mu g/m^3$ at Starke to a high of 9.12 $\mu g/m^3$ obtained on a Los Angeles cab driver (Fig. 1). The average air lead levels at each of the five sites are shown in Table 3. With the exception of the Los Angeles Office Workers, the group average air lead exposures were greater at work than at home. Respirable air lead exposures were significantly ($p < 0.5$) less than total exposures indicating that a significant quantity of the lead is contained in particles greater than 10 microns in diameter which would not penetrate the lung. The percentage retention of lead by the lung is believed to be greater than that from the gastrointestinal tract (7 p. 74). These large particles could, however, be swallowed.

The inadvertant inclusion of several heavy equipment operators at Starke and Barksdale and the inclusion of a painter and lead worker at Barksdale contributed to the wide standard deviations at these sites (Table 3). Day to day variation was substantial as shown by the average within subject standard deviation. They were: Philadelphia ± 1.113; Starke ± 0.864; Barksdale ± 1.904; Los Angeles Cab ± 2.460 and Los Angeles Office Workers ± 1.261.

Indices of Lead Absorption:

Except for one individual, the blood and urine measurements were well within the currently accepted normal limits for non-occupationally exposed people. These are: Blood Pb < 40 μg/100 gm, urine Pb < 80 μg/Liter and DALA 0.6 mg/100 ml (7, p. 251, 16). It is significant that despite air lead exposures approaching 10 $\mu g/m^3$ that only one person exceeded these values. His blood Pb was 53 μg/100 gm; urine Pb 109 μg/L; DALA 1.13 mg/100 ml; and ALAD was 3 units of activity per ml of RBC. He is believed to drink illicit moonshine whiskey and attempts to obtain samples of it for Pb analysis have been unsuccessful. Because of this history, data from this subject are not included in the air Pb comparisons. His air Pb exposure was only 1.37 $\mu g/m^3$.

Table 3 Mean subject air lead exposure ($\mu gm/m^3$ ± 1 S. D.)

Site	On Duty Total	On Duty Respirable	Off Duty Total	Combined Exposure Total	Combined Exposure Respirable
Philadelphia, Pa Cab Drivers	5.10 ± 1.11	4.34 ± .86	1.48 ± .23	2.62 ± .42	2.37 ± .34
Starke, Fla.	2.01 ± 2.52	1.39 ± 2.39	0.37 ± .31	0.81 ± .82	0.64 ± 0.78
Barksdale, Wisc.	2.84 ± 5.19	N.D.	0.36 ± 0.14	1.01 ± 1.43	N.D.
Los Angeles, Calif. Cab Drivers	9.42 ± .98	7.48 ± .92	4.22 ± 1.28	6.10 ± 1.02	5.37 ± 1.02
Los Angeles, Calif. Office Workers	3.05 ± .76	N.D.	3.07 ± .81	3.06 ± .75	N.D.

N.D. = Not determined

Table 4 shows the mean obtained for each of the biologic parameters by location. They are comparable to those reported in the literature for non-occupationally exposed groups (16–26). The differences between locations were significant ($p < 0.01$) and any two whose mean differed by more than the L.S.D. (Least Significant Different) were significantly ($p < 0.05$) different from each other. These differences, with the exception of ALAD, were significant on both the arithmetic and logarithm scale. The majority of the DALA effect is attributed to the low values found in Barksdale. The two cab studies had significantly ($p < 0.05$) lower ALAD activity than the other locations. Carbon monoxide exposure may be a contributing factor in the lower ALAD activity found in the cabdrivers and will be discussed later (see section on Effect of Smoking and Carboxyhemoglobin on ALAD).

Adjustment of the data for differences in air lead exposure, smoking differences and osmolality (urine tests only) failed to correct the significant differences in biological parameters between sites. This suggests that variables other than air lead, smoking and osmolality are effecting the data. One obvious missing variable is ingested lead.

Table 4. Mean blood and urine data (± S.D.)

Response	Philadelphia Cab Study	Starke[a] Fla.	Barksdale Wisconsin	Location Los Angeles Cab Study	Los Angeles Office Workers	LSD[b]	Site F[c]
Blood Pb (μgm/100 ml)	22.4 ± 3.3	16.4 ± 6.0	13.8 ± 6.2	24.6 ± 4.5	19.9 ± 5.0	2.6	22.12*
Urine Pb (μgm/L)	23.9 ± 5.4	13.1 ± 5.0	16.5 ± 11.0	26.1 ± 7.4	18.7 ± 5.4	3.7	16.22*
Urine DALA (mg/100 ml)	0.423 ± .116	0.352 ± .135	0.303 ± .096	0.363 ± .070	0.352 ± .094	.053	5.09*
ALAD (activity/ml RBC)	77.1 ± 23.7	99.6 ± 37.9	92.9 ± 31.8	77.4 ± 21.9	95.9 ± 30.9	15.3	3.77*
Osmolality (mOs/L)	848.6 ± 143.1	779.8 ± 182.4	808.0 ± 166.7	795.9 ± 150.0	803.1 ± 122.0	N.D.	N.S.
Creatinine (mg/100 ml)	178.2 ± 46.7	146.5 ± 44.8	154.2 ± 41.0	167.5 ± 47.6	159.2 ± 47.8	N.D.	N.S.

(a) Data from one subject omitted (see text).
(b) Least Significant Difference = any two means which differ by more than LSD are significant ($p < .05$)
(c) F statistic for significance of the difference of the five sites. * = Significant at $p < .01$.
N.S. = not significant; N.D. = not determined

Correlation Between Air Pb and Blood Pb:

Separate scatter plots for all five groups showing each individual's air Pb exposure and his corresponding blood Pb concentration are shown in Fig. 1. Statistical tests have been applied to determine the significance of the regression line of log air Pb vs. log blood Pb for each individual group. At the 95% confidence level, the slopes of these regression lines are not signifi-

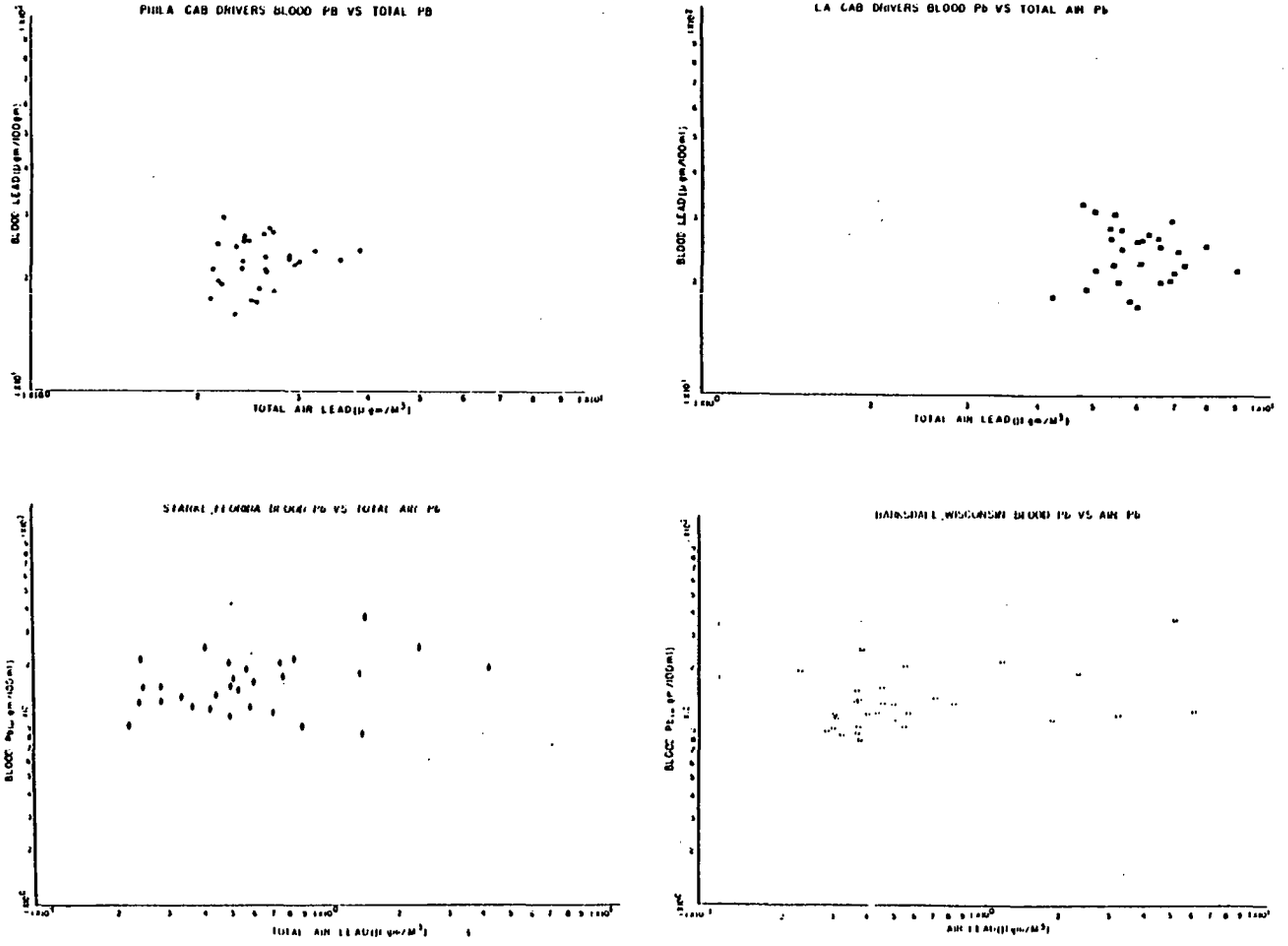

PHILA CAB DRIVERS BLOOD PB VS TOTAL PB
BLOOD LEAD(µgm/100gm)
TOTAL AIR LEAD(µgm/M³)
LA CAB DRIVERS BLOOD Pb VS TOTAL AIR Pb
BLOOD LEAD(µgm/100ml)
TOTAL AIR LEAD(µgm/M³)

Fig. 1

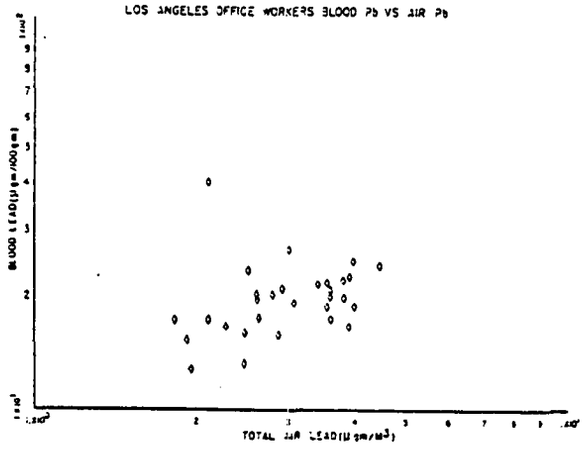


Fig. 1 (continued)

cantly different from zero, that is a horizontal line, as shown below:

Site	Log Blood Pb Intercept	Slope	95% C.L. for slope
Philadelphia	1.6258	.177	±.391
Starke	1.5430	.159	±.179
Barksdale	1.1398	.148	±.148
L.A. Cab	1.3648	-.015	±.437
L.A. Office	1.1753	.240	±.317

The lack of any significant correlation between air Pb and blood Pb indicates four possibilities: 1. there is in fact no correlation between air Pb and blood Pb; 2. thirty subjects is too few to demonstrate significance; 3. the range of data is too narrow to show significance; or 4. variables other than air lead (lead ingested from food and drink) are overwhelming any effect which air lead might have on blood lead.

From a statistical point of view, it is appropriate to combine the data and compute one overall slope for the relationship of air lead and blood lead *if it can be shown that the slopes are homogeneous.* By doing this, both the number of subjects and the range of data are increased.

An overall multiple regression analysis allowing for separate slopes and intercepts for each site showed that the slopes for each group were not significantly different from each other; i.e. the slopes were homogeneous. The *intercepts*, however, were significantly different from each other. These different intercepts indicate that variables other than air lead are affecting blood lead. Thus, the representation of the combined data for all five groups by one line could be misleading. Consider, for example, Fig. 1 a. The correlation between x and y for two populations is shown. The relationships have similar slopes but different intercepts. The dash-

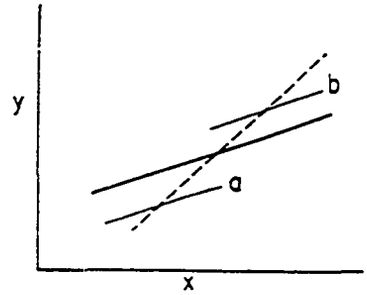


Fig. 1 a

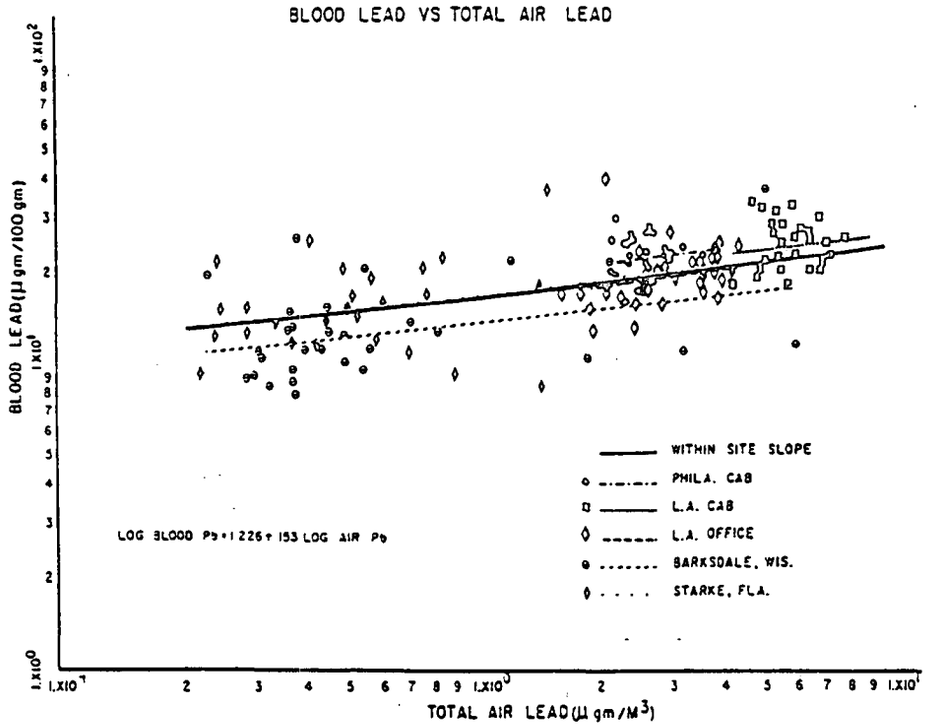


Fig. 2

ed line shows the relationship between x and y when the data from a and b are analyzed by simple regression. The heavy line shows the average relationship between x and y when different intercepts are accounted for by multiple regression techniques.

Since the individual slopes of the five groups are homogeneous, a multiple regression analysis was made of the data from 149 subjects to obtain the best average slope. In this analysis dummy variables were used to account for the different intercepts. Fig. 2 shows that the data tended to clump into five subgroups by location. The average relationship between air Pb exposure and blood Pb concentration obtained by drawing a line with a slope of 0.153 through the average blood lead concentration for 149 subjects, is defined by the equation: log blood Pb = 1.2257 + 0.153 log air Pb. The slope of this regression was significantly ($p < 0.01$) different from zero (95% Confidence Limits, C. L. = ± 0.079). Approximately 56% of the variance in blood Pb is not explained by air Pb ($R^2 = 0.436$).

Figure 2 also shows the regression lines obtained when the data from each site are adjusted to the common slope of 0.153. This is justified since the slopes are homogeneous. This plot clearly illustrates that the model which gives the best fit to the data is not a single line but a series of lines having similar slopes with different intercepts. The different intercepts indicate that variables other than air Pb are affecting blood Pb.

The slope of this line (0.153) is less than that found by GOLDSMITH and HEXTER (0.243) [2] and considerably

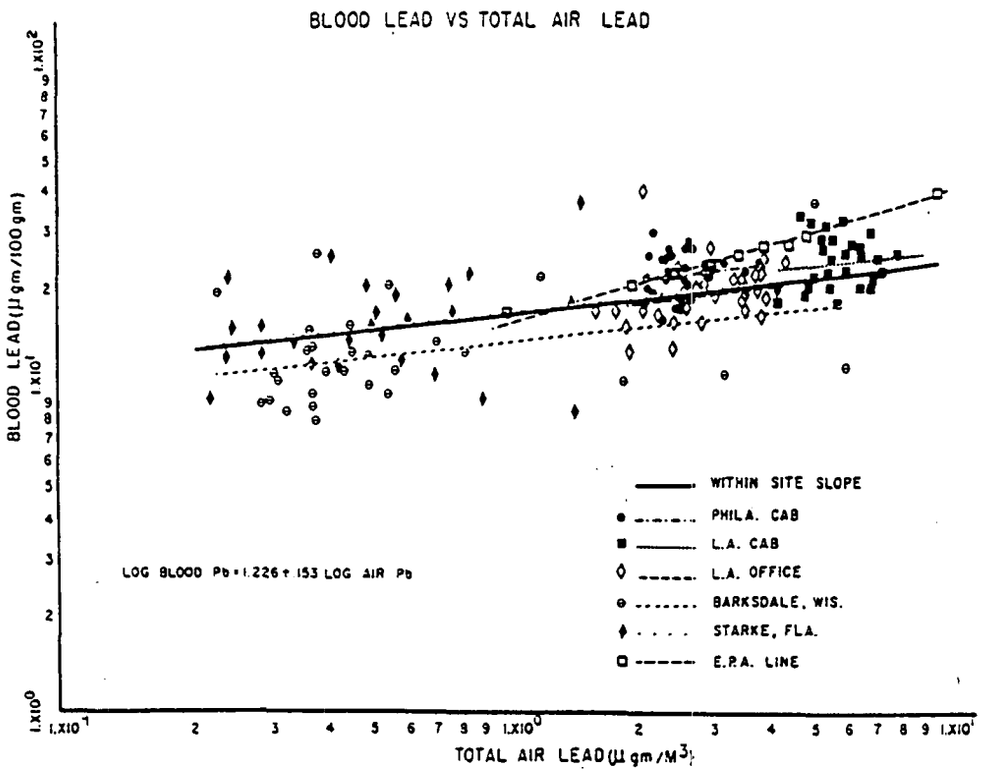


Fig. 3

less than that based on the theoretical calculations of the Environmental Protection Agency (27), Fig. 3. Respirable air Pb exposures were available on 89 subjects. A multiple regression analysis, using dummy variables to represent the different intercepts, indicated that the slope (0.112) of the log respirable air lead – log blood lead line was significantly ($p < 0.05$) different foom zero.

It should be noted that any attempt to predict blood lead levels based solely on the use of the average relationship line developed in this study could be misleading because the effect of lead intake from other sources, such as food and drink, is significant. For example, analyses of the data show that this average relationship line with a slope 0.153 accounts for only 44 percent of the variation in blood lead. Furthermore, the fact that the intercepts of the individual lines through the five groups are different is evidence that variables other than air lead are influencing blood lead levels. All this emphasizes the importance of considering all sources of lead intake in any attempt to predict blood lead levels.

Correlation Between Air Pb and Other Indices (Urine Pb, ALAD, DALA):

Statistical tests for significance of the linear regression of log air Pb vs log urine Pb have shown that the only regression lines significantly ($p < 0.05$) different from zero were those at Starke and Barksdale (Fig. 4). The slopes from

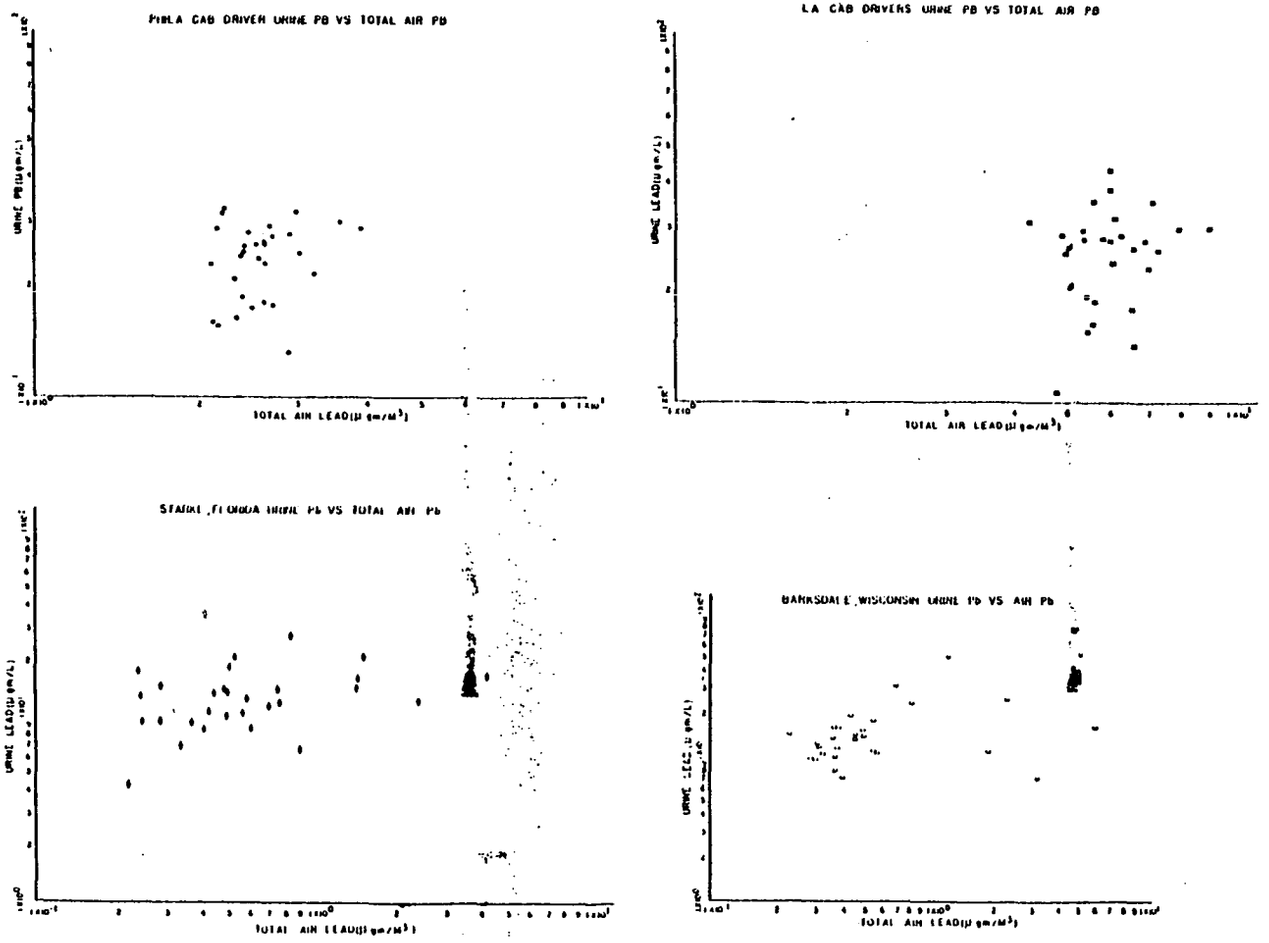

PUBLA CAB DRIVER URINE PB VS TOTAL AIR PB
LA CAB DRIVERS URINE PB VS TOTAL AIR PB
STARKE, FLORIDA URINE PB VS TOTAL AIR PB
BARKSDALE, WISCONSIN URINE PB VS AIR PB
TOTAL AIR LEAD(μgm/M³)

Fig. 4

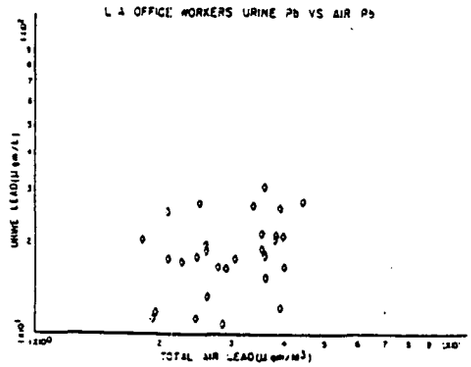


Fig. 4 (continued)

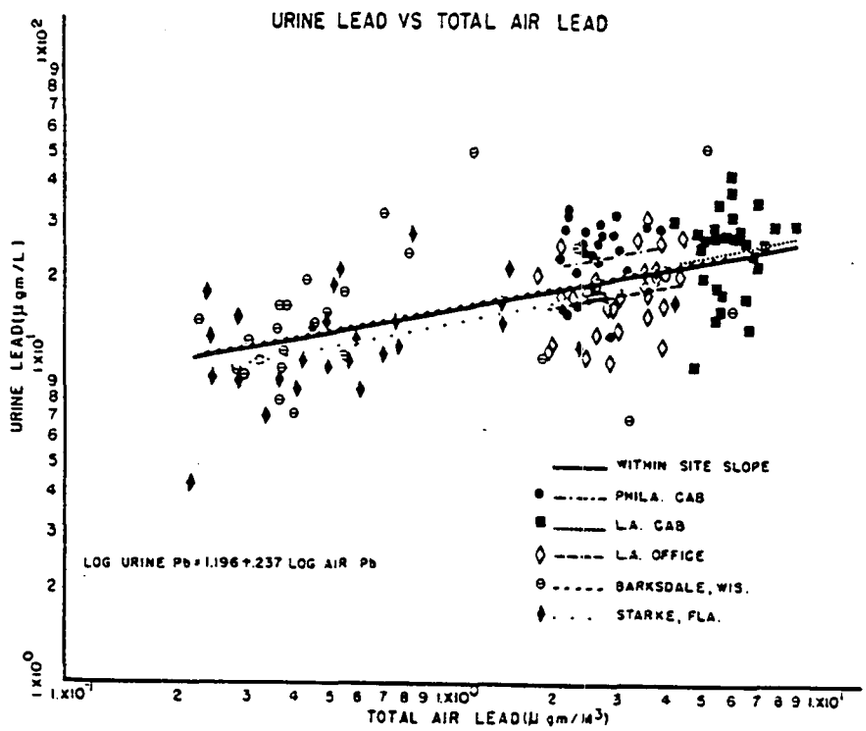


Fig. 5

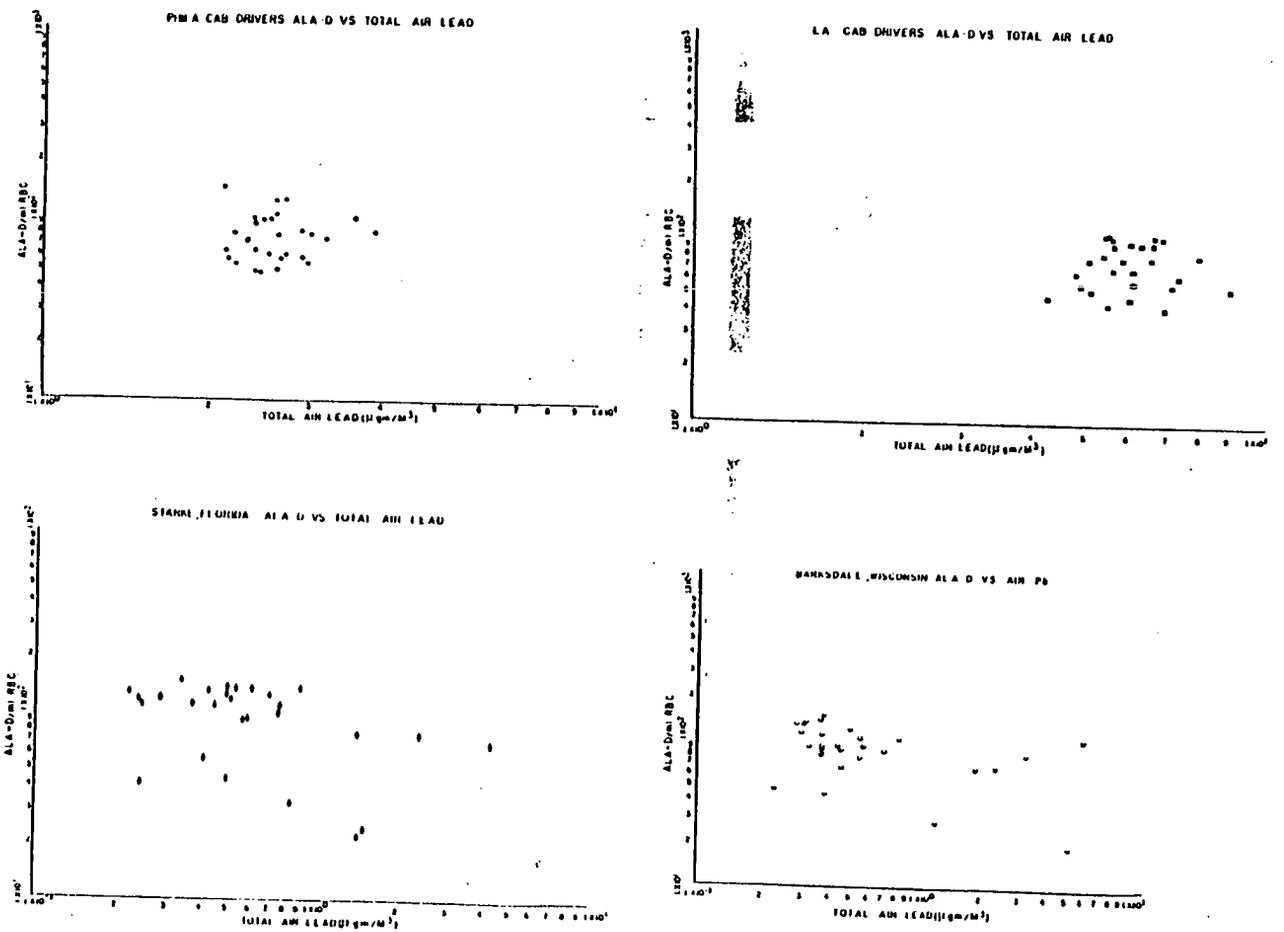

PHILA CAB DRIVERS ALA-D VS TOTAL AIR LEAD
LA CAB DRIVERS ALA-D VS TOTAL AIR LEAD
STARKE, FLORIDA ALA-D VS TOTAL AIR LEAD
BANKSDALE, WISCONSIN ALA-D VS AIR Pb
ALA-D/ml RBC
TOTAL AIR LEAD(μgm/m³)

Fig. 6

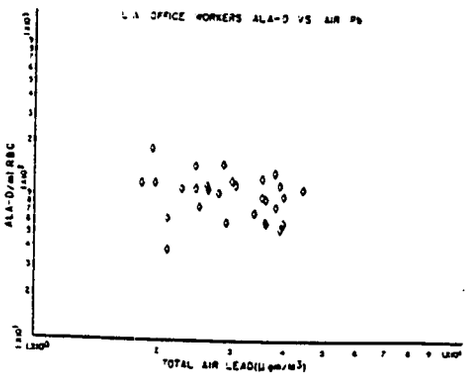


Fig. 6 (continued)

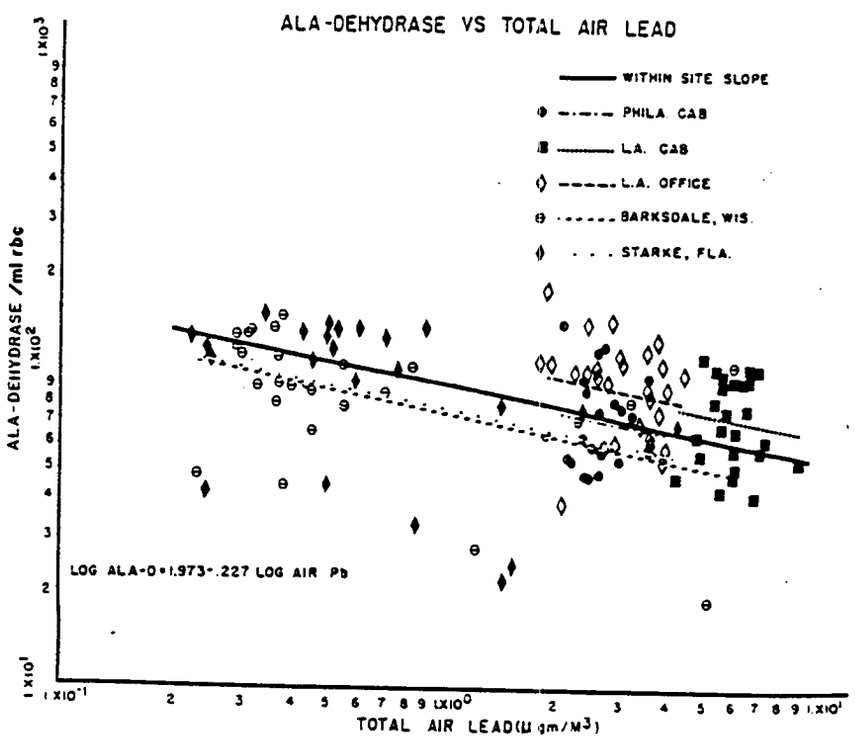
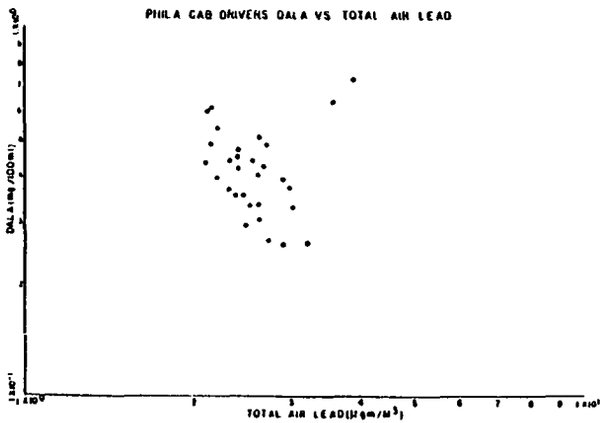
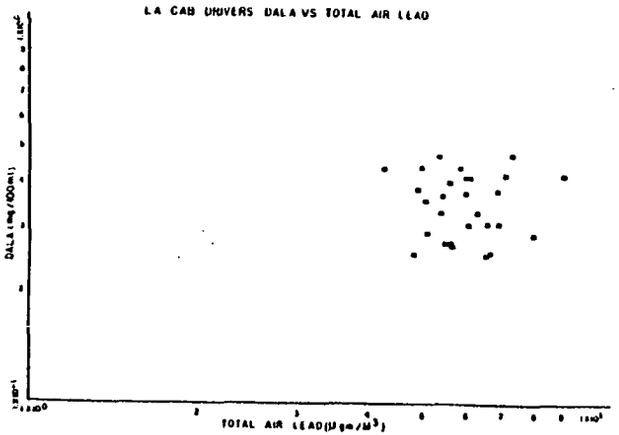
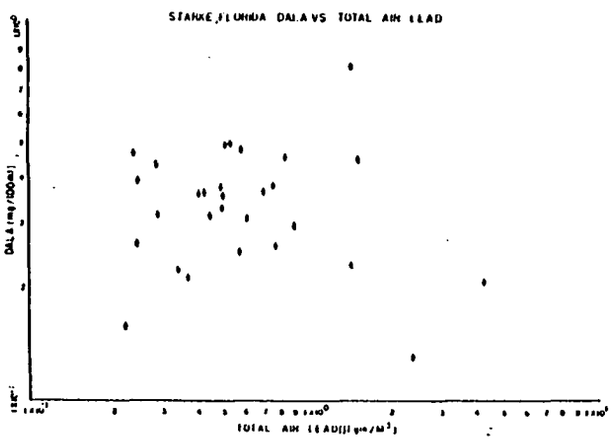


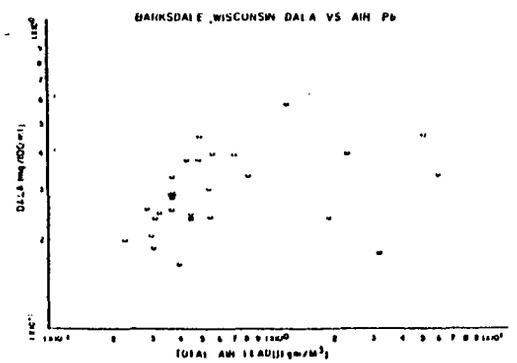
Fig. 7

FIG. 8


PHILA CAB DRIVERS DALA VS TOTAL AIR LEAD
DALA (mg/100ml)
TOTAL AIR LEAD(μgm/M³)


LA CAB DRIVERS DALA VS TOTAL AIR LEAD
DALA (mg/100ml)
TOTAL AIR LEAD(μgm/M³)


STARKE,FLORIDA DALA VS TOTAL AIR LEAD
DALA (mg/100ml)
TOTAL AIR LEAD(μgm/M³)


BANKSDALE,WISCONSIN DALA VS AIR Pb
DALA (mg/100ml)
TOTAL AIR LEAD(μgm/M³)

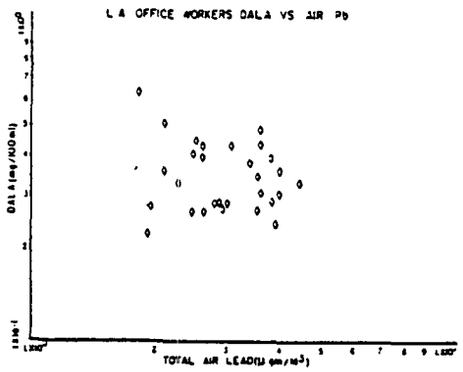


Fig. 8 (continued)

the five groups were found to be homogeneous. Fig. 5 shows the data from all 149 participants. The average relationship between log air Pb and log urine Pb is defined by the equation: log urine Pb = 1.1959 + 0.237 log air Pb. The slope of this regression was significantly ($p < 0.01$) different from zero (95 C. L. = ± 0.093). Approximately 60% of the variance in urine Pb is not explained by air Pb (R^2 = 0.402). The similarity between this relationship and that of air Pb vs blood Pb (Figure 2) is apparent.

As with urine Pb, statistical tests for significance of the linear regression of log air Pb vs log ALAD have shown that the only regression lines signifi-

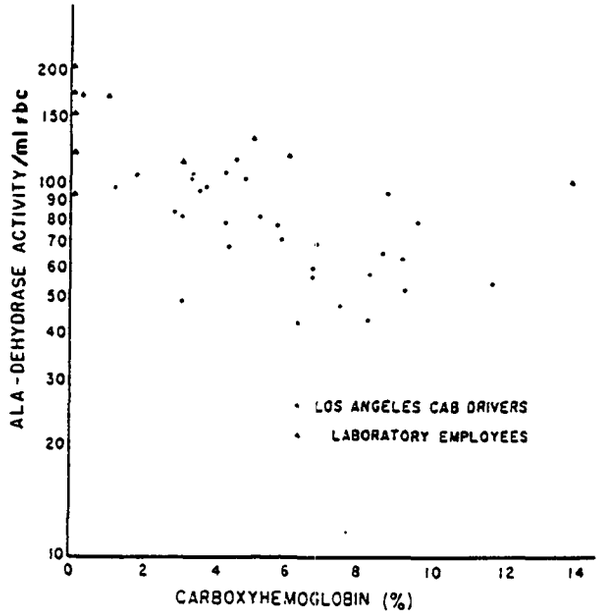


Fig. 9

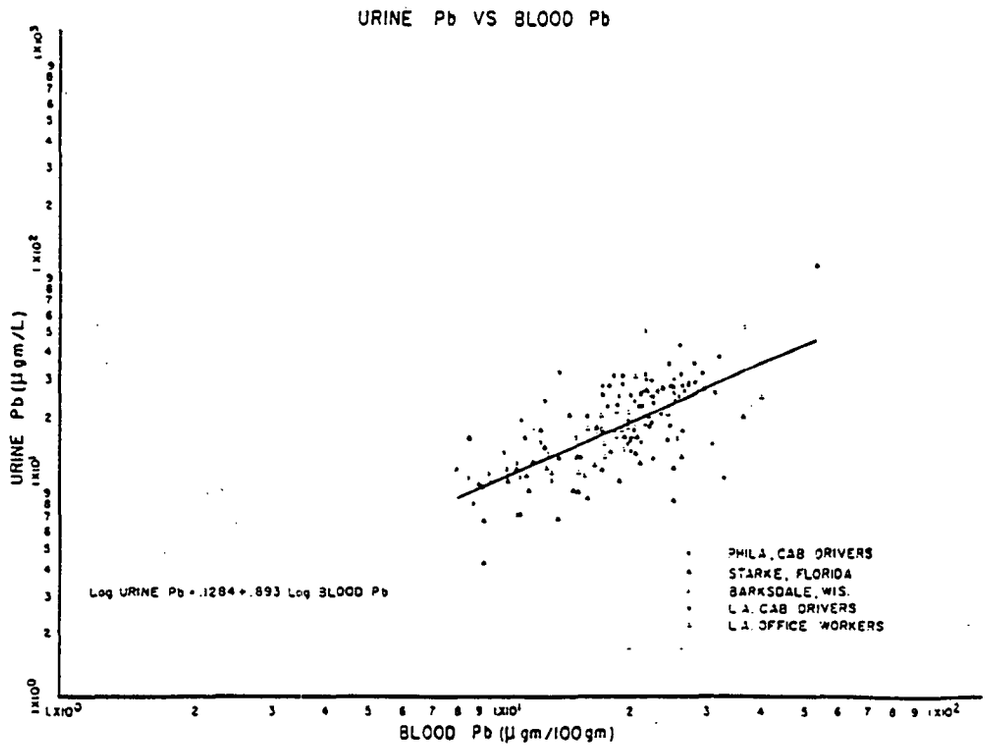


Fig. 10

cantly ($p < 0.05$) different from zero were found at Starke and Barksdale (Fig. 6). The slopes from the five sites were homogenous and Fig. 7 shows the data of the 149 subjects. The average relationship between log air Pb and log ALAD is defined by the equation: log ALAD = 1.9731 − 0.227 log air Pb. The slope of this regression was significant ($p < 0.01$) and the 95% C. L. were ± 0.115. Unlike blood Pb and urine Pb, approximately 93% of the variance in ALAD activity is not explained by air Pb ($R^2 = 0.072$), suggesting that variables other than air Pb are significantly affecting ALAD.

Statistical tests for significance of the regression of log air Pb vs log DALA showed that none of the regression lines had slopes significantly ($p < 0.05$) different from zero (Fig. 8). This was also true when the data from the 149 subjects was examined.

Effect of Smoking and Carboxyhemoglobin on ALAD:

Smoking was found to significantly ($p < 0.01$) depress ALAD activity (Table 5). This was true even after the data were adjusted for air Pb and location differences.

Table 5 Effect of smoking on ALA-Dehydrase

Smoking Category	Log ALA-Dehydrase[1]	Detransformed
Nonsmokers	1.9610	91.4
< 1/2 pack/day	1.9999	100.0
1/2-1 pack/day	1.8597	72.4
1 or more packs/day	1.8972[2]	78.9
Cigars	1.7893[2]	61.6
Smoking F	5.31**	

**Significant at the .01 probability level
[1] Adjusted for log total air Pb and site differences
[2] Significantly different from nonsmoker average

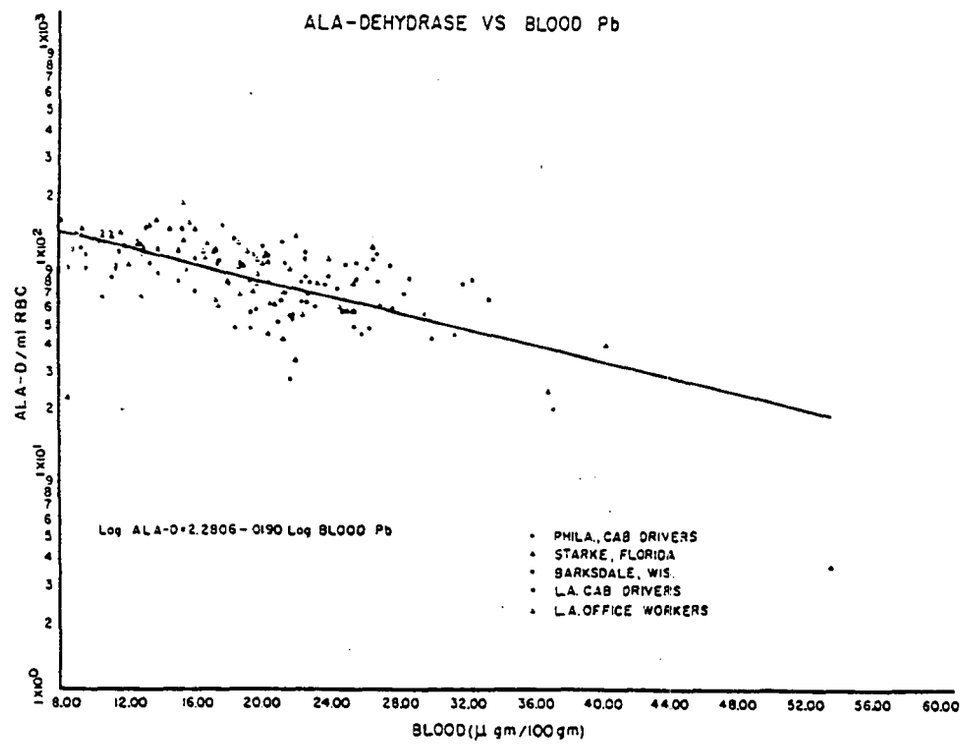


Fig. 11

Carboxyhemoglobin (COHb) determinations were done on the blood specimens of the L. A. cab drivers. These ranged from 3 to 11%. To increase the range of data, COHb determinations were made on 11 laboratory personnel on whom blood Pb and ALAD data existed. Both sets of data were analyzed separately and combined. No significant correlation between blood Pb and ALAD was found in either group because of the narrow range of data at each site. When the data were combined, both blood Pb and COHb were found to significantly ($p < 0.01$) depress ALAD activity:

Approximately 61% ($R^2 = 0.61$) of the varance in ALAD is attributed to COHb and blood Pb with each accounting for about 30% of the variance. No significant interaction between blood Pb and COHb was found. Thus, the effects of COHb and blood Pb on ALAD activity are significant and of equal magnitude. Fig. 9 is a plot of COHb vs ALAD. This effect of COHb on ALAD may be influencing the lower ALAD activity of occupationally exposed cab drivers compared to non-occupationally exposed Du Pont employees.

$$\log \text{ALAD} = 1.9401 - 0.0814 \frac{\text{COHb} - 4.91}{3.43} - 0.0804 \frac{\text{Blood Pb} - 21.58}{6.54}$$

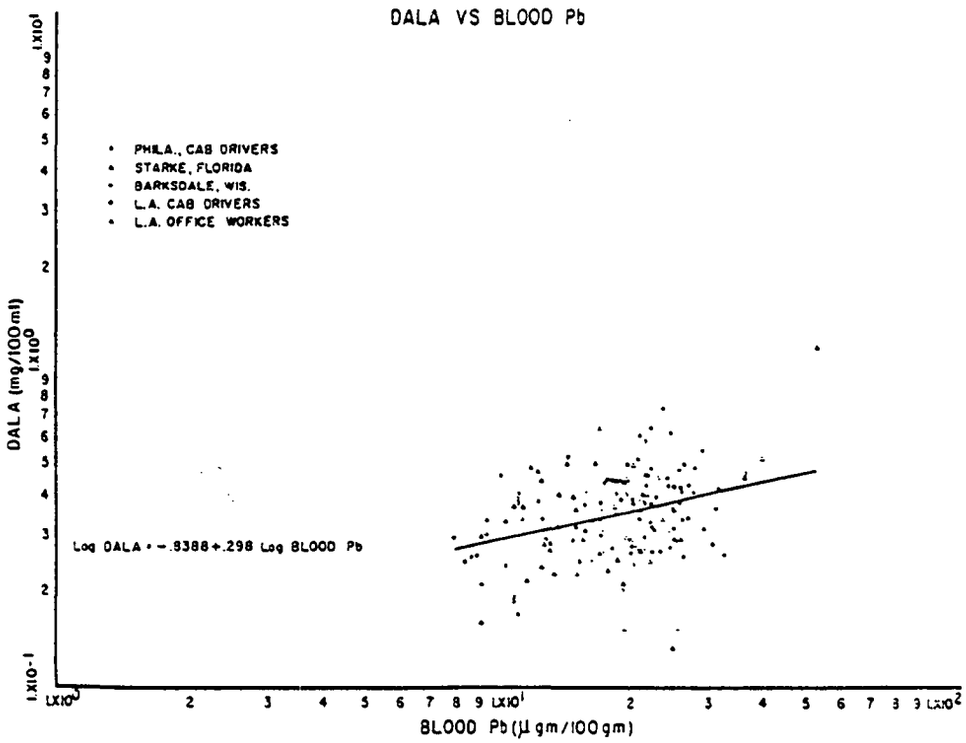


Fig. 12

Interrelationship Between Indices of Pb Absorption:

There was a significant ($p < 0.01$) correlation between blood Pb and urine Pb (Fig. 10) with 47% of the variance in urine Pb being correlated with blood Pb ($R^2 = 0.47$).

A significant ($p < 0.01$, $R^2 = 0.41$) negative correlation was found between blood Pb and ALAD (Fig. 11). This agrees very closely with that described by HERNBERG *et al.* (28) which was log ALAD = 2.274 − 0.018 blood Pb. A curvilinear relationship similar to that described by HAEGER-ARONSEN *et al.* (18) between blood Pb and ALAD was not possible due to the lack of blood Pb values above 40 μg/100 gm.

The relationship between blood Pb and DALA was significant ($p < 0.01$, $R^2 = 0.11$) and is shown in Fig. 12. Here too, the lack of blood Pb concentrations above 40 μg/100 gm did not permit the description of a curvilinear relationship such as that described by SELANDER and CRAMER (16). The slope of our line on an arithmetic plot was 0.0072 which is almost identical to the 0.007 reported by SELANDER and CRAMER (16) for blood Pb values less than 40.

The relationship between ALAD and DALA is shown in Fig. 13. The lack of high DALA values prevented the description of any curvilinear relationship. HAEGER-ARONSEN *et al.* (18) reported a curvilinear relationship between ALAD and DALA; however, they had DALA excretions as high as 5.5 mg/100 ml.

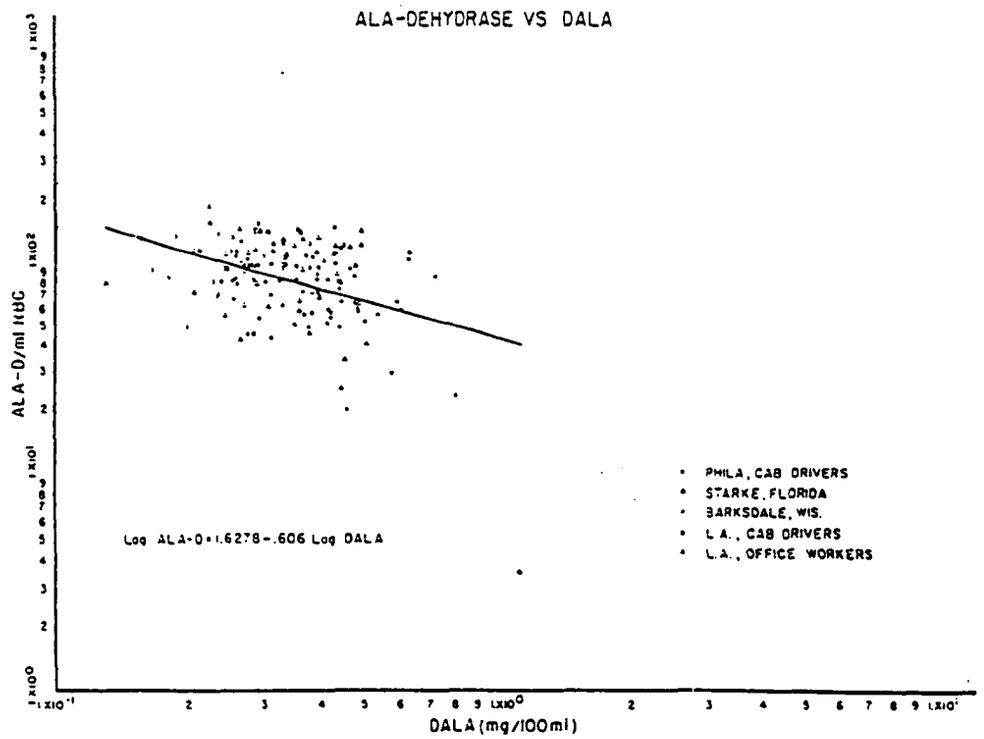


Fig. 13

Other Variables:

An overall regression analysis which included all of the variables in the study showed that age, years of service, and water Pb had no significant effect on blood Pb, urine Pb, ALAD or DALA. There were, however, significant differences among the average water Pb concentrations of the four groups. Each subject, except those in Philadelphia, furnished one sample of their home drinking water for Pb analysis.

Afternoon urine Pb concentrations were significantly ($p < 0.01$) higher than morning values for both of the Los Angeles groups studied. DALA excretion was significantly ($p < 0.01$) higher in the afternoon specimen of only the L. A. cab drivers. This DALA difference was no longer significant when corrected for osmolality.

Discussion

This study represents the first time that personal air samplers have been used to monitor the concentration of substances found in the community air. They have the distinct advantage of giving an individual's exposure rather than relying on data obtained from a stationary sampler located on a rooftop or on street level. This viewpoint is substantiated by the marked differences found in our study in the air lead exposures of individuals living in the same city. Hence, the average air lead exposure in a city does not accurately reflect the air lead exposure of individuals at that site. This was particularly noticeable at lower ambient air lead exposures such as those seen at Starke, Florida and Barksdale, Wisconsin, Fig. 2 shows that the air lead exposures at the other sites tended to clump into a narrow range of values: whereas, those at Starke and Barksdale covered a much wider range of values.

The use of different occupational groups located in different cities; studying each group at a different time; the lack of data relative to ingested Pb; and the lack of detailed histories and physical examinations are obvious design deficiencies in this study. The use of different occupational groups in different cities may have influenced the data in some way that we are unaware of at the present time. These different groups may have habits or characteristics other than different air lead exposures which are affecting their blood Pb. The failure of the blood Pb values to equalize when corrected to a common air lead strongly suggests that, indeed, some variable other than air Pb exposure is effecting the blood Pb. One obvious missing variable is data relevant to ingested lead. The importance of sources of lead exposure other than air Pb is most vividly pointed out by the finding that the only obviously abnormal blood and urine responses were found in an individual believed to drink moonshine whiskey and not as a result of his air lead exposure. The concentration of lead in moonshine whiskey may exceed 1,000 μg/liter (7, p. 240).

The carrying out of the study during different times causes concern about analytical variation. Although attempts were made to keep the procedures constant, unexpected changes did occur as evidenced by the change in DALA analysis which occurred midway through the study (see methods). It was possible to obtain two blood and urine specimens from 29 out of 30 of the participants at Starke, Florida, approximately 7 months after the original study. The blood Pb concentrations agreed well with those obtained earlier as shown below.

	June 1970	February 1971	Difference ± 95% Confidence Limits
Blood Pb	17.8	17.4	−0.4 ± 1.8
Urine Pb	16.6	17.7	1.1 ± 3.1

Analysis of the logarithms of the urine Pb and blood Pb data also showed that there was no significant difference June 1970 and February 1971 results.

The lag time between exposure to air Pb and its reflection in the blood and urine is of concern. KEHOE (29) reported a definite and prompt increase in urine Pb excretion within a few days following the exposure of experimental subjects to air Pb. COULSTON (30) found a rise in blood Pb as early as one week after the initiation of experimental human exposures to airborne Pb. We believe that the fact that our subjects have been living and working at the same place for many years has resulted in some equilibrium between their exposure and blood and urine responses. Thus, our subjects are not suddenly exposed to 6 $\mu g/m^3$ lead from a background of 0.1 $\mu g/m^3$.

Blood and urine lead concentrations have been reported to be higher during summer months (39). The influence of this variable on our data is not known. Also not known, is the precise effect of vascular fluid shifts on biologic indices of lead absorption. Prior studies have shown that DALA concentration is influenced by osmolality (31). In this regard, correction of our urine data for osmolality did not change the fact that there was a significant correlation between air Pb exposure and urine Pb concentration. It is surprising that GOLDSMITH and HEXTER (2) found any relationship between air Pb exposure and blood Pb concentration in view of the fact that the air Pb exposures were estimated and that data from different laboratories was used. STOPPS (3) has criticized the statistical approach used by GOLDSMITH and HEXTER. He states "To allow such group averages to be used to calculate a linear regression line. individual regression lines should have been fitted to each of the groups of data points comprising the population representing each subpopulation. These individual regression lines should then be subjected to the following three tests before a single regression line can be fitted: 1. the variance about each of the regression lines must be similar: 2. the slopes of the regression lines must be the same, that is to say, they can be considered paralleled: 3. the separate parallel lines must be shown to be segments of one straight line." In this study, the variances about the lines were similar, and the slopes homo-

geneous, however the intercepts were not homogeneous.

The slope of our regression line describing the relationship between air Pb and blood Pb is less than that reported by GOLDSMITH and HEXTER (2) and is considerably less than that based on theoretically calculated data points by the Environmental Protection Agency (27).

The health significance of finding a decreased level of ALAD activity is not known. It has been suggested that this inhibition is an in-vitro phenomenon and that the body has sufficient enzyme reserve to meet its needs (32, 7, p. 227). Studies in our laboratory (33) have shown that rats and dogs fed lead acetate in their diet for two years had significantly depressed ALAD activity at a blood Pb of approximately 75 μg/100 ml. This depression of ALAD activity had no effect on the mortality of the animals, their clinical laboratory tests or behavior, neurologic examination or any effect on reproduction. Higher doses of lead in the feed were associated with changes in DALA, mortality and other effects. The blood Pb concentrations at these higher levels of lead in the feed were about 80 μg/100 ml.

Since ALAD is believed to be involved in hemoglobin synthesis, another study was carried out to determine if having a depressed level of ALAD would interfere with the ability to make hemoglobin under a stressful situation such as hemorrhage (34). Dogs with markedly depressed levels of ALAD activity were subjected to severe hemorrhage. They regenerated their hemoglobin just as rapidly as control dogs subjected to the same procedure. These two studies support the hypotheses of enzyme reserve and are in conflict with the health significance, if any, of a depressed level of ALAD.

The finding that increasing levels of carboxyhemoglobin in vivo are correlated with a fall in ALAD activity is novel, as is the depression of ALAD activity with Smoking. RAUSA et al., (35) have shown that carbon monoxide accentuates the in vitro depression of ALAD by lead. We have exposed rats to 250 ppm carbon monoxide for four hours a day, five days a week, for four weeks without seeing any decrement in ALAD activity (41). The response, however, may be species dependent or require a more prolonged exposure. Alcohol ingestion, copper, mercury, silver, manganese, and cobalt have also been shown to effect ALAD activity (36, 37). We did not examine these variables in the present study; however, the finding that 93% of the variance in ALAD activity is not explained by air Pb exposure suggests that the role of other variables in depressing ALAD requires further study.

GOLDSMITH (38) states that any change in blood Pb concentration constitutes a significant health effect and that this should form the basis for an air Pb standard. STOPPS (3) and more recently ENTERLINE (4) believe that it would be more appropriate to choose air Pb level which gives an intolerable response and letting that be the maximum permissible level. It is generally agreed that there is no demonstrable *in-vivo* effect associated with blood Pb concentrations below 40 μg/100 gm and that minimal subclinical metabolic effects are seen in the 40 to 60 μg/100 gm range (7, p. 251). Clear cut clinical signs and symptoms are almost always associated with blood Pb concentrations greater than 80 μg/100 gm. (7, p. 229).

It is significant that during the present study only one subject out of 150 had a blood Pb concentration exceeding 40 μg/100 gm and this was attributed to factors other than air Pb exposure. The other 149 individuals had time-weighted air Pb exposures as high as 9.12 $\mu g/m^3$ with blood Pb concentrations below 40 μg/100 gm. Also significant, is the fact that the average air Pb exposure of cab drivers in Los Angeles during the study period was 6.10 $\mu g/m^3$ and their blood Pb concentration averaged 24.6 μg/100 gm which is well below 40 μg/100 gm.

Summary

The correlation between levels of atmospheric lead found in community

air and indices of lead absorption such as blood Pb, urine Pb, DALA and ALAD activity was studied in five groups representing a total of 150 individuals using personal air sampling equipment. The air lead exposure of these individuals was measured continuously, 24 hours per day, for periods of time ranging from two to four weeks. During this time blood and urine specimens were obtained for the analyses indicated. When the blood lead concentration of each 30 individuals was compared to their corresponding air lead exposure, the slope of the resulting regression line was not significantly different from zero, indicating no correlation between air lead and blood lead within each group. Analysis of the data from 149 of the subjects resulted in a slight but statistically significant slope. Although this line represents the best available relationship between air lead and blood lead for the data developed in this study, its use for predicting blood leads could be misleading because of the importance and variability of lead intake from other sources.

A similar correlation between air Pb exposure and urine Pb was found. An even smaller correlation was found between air lead exposure and ALAD activity. There was no correlation between air lead exposure and DALA excretion. A negative correlation was found with increased smoking vs ALAD and increased carboxyhemoglobin vs ALAD. Despite air lead exposures approaching 10 $\mu g/m^3$, only one individual had abnormal blood and urine responses. These were attributed to factors other than air lead exposure.

Acknowledgements

The authors wish to thank Drs. D. R. Diggs and G. J. Stopps for their guidance during this study. The blood and urine lead analyses were carried out by Dr. L. A. Williams and the air filters were analyzed by E. Lindemanis. DALA, ALAD, COHb, creatinine and osmolality determinations were done by the Biochemistry Section at Haskell Laboratory. Special thanks are given to J. K. Livingstone and C. T. Kunkel, Jr., who served as on-site project coordinators.

Individual Subject Means Used in Analyses

Dupont environmental lead studies
Philadelphia cab study DATA

Subject	On duty		Off duty	Combined exposure		DALA	Creatinine	Osmolality	ALA-Dehydrase	Urine PB	Blood PB
	Resp PB	Total PB	Total PB	Resp PB	Total PB						
1	4.32	4.95	1.66	2.53	2.73	.27	149	791	122	17	18
2	3.88	5.41	1.18	1.91	2.33	.37	186	815	70	20	15
3	7.35	8.92	1.26	3.10	3.60	.63	294	1069	98	29	22
4	4.49	5.18	1.18	2.20	2.42	.47	169	735	89	25	26
5	6.24	6.67	1.61	3.08	3.22	.26	121	648	75	21	23
6	3.94	4.29	1.31	2.01	2.11	.43	212	995	143	22	17
7	3.51	4.88	1.94	2.55	3.03	.33	142	853	79	24	22
8	5.76	7.87	1.59	3.10	3.91	.73	248	1051	83	28	23
9	4.71	5.56	1.36	2.37	2.63	.33	171	1035	119	26	21
10	4.77	5.43	1.63	2.76	2.99	.37	153	890	54	31	21
11	4.58	5.71	1.75	2.57	2.92	.39	217	946	59	27	23
12	4.46	5.06	1.44	2.51	2.73	.48	231	1038	59	27	26
13	3.62	4.17	2.00	2.62	2.69	.42	204	848	58	29	27
14	4.12	4.59	1.52	2.40	2.57	.44	178	968	95	23	18
15	4.27	5.01	1.31	2.19	2.42	.42	120	910	48	24	25
16	3.97	4.50	1.42	2.07	2.21	.40	132	896	79	31	19
17	4.73	5.45	1.41	2.33	2.55	.33	193	844	60	26	17
18	4.25	5.21	1.17	2.18	2.50	.29	175	781	93	17	17
19	5.16	5.69	1.33	2.47	2.63	.40	132	828	100	17	26
20	4.17	4.47	1.22	2.08	2.17	.61	196	819	56	28	24
21	3.68	3.97	1.63	2.14	2.23	.54	245	826	54	32	29
22	3.61	4.73	1.22	1.97	2.34	.44	210	860	72	16	24
23	3.91	4.40	1.62	2.47	2.64	.51	208	891	49	23	20
24	4.61	5.04	1.67	2.74	2.91	.26	84	402	81	13	22
25	3.37	3.73	1.49	2.05	2.17	.49	171	815	57	15	19
26	3.81	3.86	1.60	2.38	2.40	.45	207	849	63	18	22
27	3.59	5.07	1.10	1.91	2.40	.36	190	967	96	24	21
28	3.76	4.27	1.32	1.95	2.13	.60	102	588	63	15	21
29	3.93	4.62	1.64	2.39	2.64	.31	144	816	78	25	22
30	3.61	4.18	1.68	2.28	2.47	.35	145	670	48	28	25

Dupont environmental lead studies
Starke, Florida DATA

Subject	On duty		Off duty	Combined exposure		DALA	Creatinine	Osmolality	ALA-Dehydrase	Urine PB	Blood PB
	Resp PB	Total PB	Total PB	Resp PB	Total PB						
1	.11	.30	.22	.20	.24	.27	134	843	42	12	21
2	1.39	1.66	.12	.44	.50	.36	192	1000	140	13	15
3	1.61	2.00	1.16	1.27	1.37	1.13	145	700	3	109	53
4	.19	.41	.20	.19	.25	.39	179	844	111	9	15
5	.34	.67	.26	.27	.34	.23	126	730	152	7	13
6	.54	.82	.21	.30	.37	.21	83	610	113	9	11
7	.34	.62	.14	.18	.24	.47	193	1008	116	17	12
8	.32	1.37	.20	.23	.50	.38	117	713	45	14	20
9	.39	.77	.29	.32	.41	.36	139	690	57	8	25
10	.64	1.08	.67	.66	.78	.26	145	614	111	12	17
11	1.03	1.90	.12	.36	.59	.48	184	1040	94	12	12
12	.55	.94	.36	.42	.54	.50	246	1019	138	21	14
13	1.35	2.06	.24	.56	.76	.38	161	647	101	14	20
14	6.84	7.95	.29	2.10	2.41	.13	53	319	78	12	25
15	4.12	4.75	.35	1.30	1.46	.81	168	683	22	16	8
16	.72	1.07	.43	.61	.61	.31	152	865	138	8	16
17	.56	3.60	.55	.55	1.53	.45	169	717	24	21	36
18	4.16	4.97	.19	1.24	1.45	.23	113	724	79	14	18
19	11.35	12.14	1.47	4.07	4.28	.21	91	864	71	17	19
20	.06	.45	.15	.13	.22	.16	85	373	127	4	9
21	.89	1.49	.77	.79	.91	.30	112	893	139	6	9
22	.19	.66	.33	.29	.43	.36	118	832	134	10	11
23	.58	1.05	.25	.36	.50	.33	119	555	126	10	10
24	.80	1.21	.24	.40	.52	.50	221	1052	119	18	16
25	.19	.41	.23	.22	.29	.32	176	725	121	9	15
26	.35	1.31	.14	.20	.45	.32	128	877	111	13	13
27	.09	.40	.25	.20	.29	.44	222	962	117	14	12
28	.98	1.62	.56	.67	.85	.46	140	749	33	27	22
29	.63	1.56	.26	.39	.71	.37	162	893	127	11	11
30	.48	1.05	.42	.43	.57	.25	116	758	93	10	19

Dupont environmental lead studies
Barksdale Wisconsin DATA

Subject	On duty		Off duty	Combined exposure		DALA	Creatinine	Osmolality	ALA-Dehydrase	Urine PB	Blood PB
	Resp PB	Total PB	Total PB	Resp PB	Total PB						
1		.46	.28		.33	.24	129	816	91	10	8
2		.29	.39		.37	.29	149	923	139	13	13
3		1.18	.37		.57	.40	230	949	93	10	11
4		.60	.42		.46	.24	129	807	67	14	12
5		.73	.16		.31	.24	136	746	134	11	10
6		1.86	.25		.71	.40	199	1031	86	32	13
7		.58	.48		.50	.46	186	1019	120	13	10
8		1.24	.33		.55	.30	140	767	106	11	9
9		.40	.27		.30	.21	144	857	112	9	9
10		.74	.23		.37	.29	138	722	81	16	15
11		2.99	.65		1.24	.58	199	892	28	50	21
12		.60	.31		.38	.29	127	647	44	16	25
13		.60	.29		.37	.33	210	988	91	10	9
14		17.96	.30		5.19	.46	186	958	19	52	37
15		1.61	.17		.65	.24	141	790	79	17	20
16		.60	.21		.31	.19	117	627	131	12	11
17		10.56	.67		3.24	.18	77	445	83	7	11
18		.77	.24		.37	.28	118	635	94	10	13
19		6.81	.26		1.90	.24	116	802	66	11	10
20		.79	.32		.44	.38	234	918	93	19	11
21		.58	.46		.50	.38	185	810	121	15	12
22		.98	.27		.46	.25	142	576	89	13	15
23		.36	.41		.40	.17	95	761	91	7	11
24		2.20	.34		.83	.33	209	1085	105	23	12
25		21.44	.62		6.08	.34	150	965	107	16	11
26		7.23	.65		2.33	.40	180	1038	68	25	18
27		.37	.38		.38	.29	195	841	150	11	8
28		.33	.20		.23	.20	119	714	48	14	19
29		.16	.45		.37	.25	105	469	111	8	8
30		.14	.34		.29	.26	128	629	130	9	9

Dupont environmental lead studies
Los Angeles cab study DATA

Subject	On duty		Off duty	Combined exposure		DALA	Creatinine	osmolality	ALA-Dehydrase	Urine PB	Blood PB
	Resp PB	Total PB	Total PB	Resp PB	Total PB						
1	8.19	9.70	2.62	4.58	5.12	.30	75	673	53	20	21
2	8.38	10.49	3.97	5.77	6.63	.31	146	711	97	26	25
3	8.17	9.61	7.15	7.50	7.99	.29	125	584	82	30	25
4	7.86	10.33	3.34	5.13	6.10	.31	167	886	69	23	22
5	6.60	9.17	3.54	4.58	5.49	.38	167	801	107	19	22
6	6.45	8.15	3.17	4.33	4.94	.39	137	830	57	28	19
7	7.13	8.91	3.84	4.97	5.51	.28	59	487	44	15	31
8	7.86	8.87	3.44	5.07	5.44	.34	149	810	106	28	26
9	8.21	9.73	2.99	4.86	5.40	.48	221	1013	83	29	28
10	6.93	8.64	4.65	5.44	6.05	.38	212	917	97	27	17
11	7.53	9.36	5.55	6.28	6.95	.31	137	454	42	27	29
12	8.42	9.87	4.71	6.03	6.55	.26	151	658	79	17	26
13	7.39	9.26	3.37	4.90	5.60	.28	123	777	103	16	20
14	6.17	9.59	4.87	5.35	6.64	.26	148	769	107	14	20
15	7.70	9.23	4.30	5.48	6.02	.42	172	825	81	38	32
16	9.16	10.32	4.16	5.90	6.30	.34	165	900	96	28	27
17	7.70	8.77	2.70	4.67	5.10	.36	199	792	78	26	31
18	7.26	8.20	3.39	4.68	5.01	.45	214	855	116	25	20
19	6.72	9.61	3.37	4.61	5.67	.27	105	622	94	18	24
20	6.46	8.23	4.41	5.22	5.89	.46	207	993	78	27	18
21	5.44	6.42	3.01	3.92	4.28	.44	184	781	48	31	18
22	8.70	10.70	8.21	8.47	9.12	.43	193	835	54	29	21
23	8.72	11.29	5.27	6.50	7.34	.48	255	936	63	25	22
24	6.69	8.36	3.11	4.27	4.83	.26	112	506	65	10	33
25	8.42	10.76	5.00	6.15	6.91	.39	158	856	104	24	20
26	8.72	9.89	5.54	6.66	7.05	.40	161	933	71	23	21
27	6.69	10.07	5.60	5.95	7.15	.43	227	823	57	35	24
28	7.16	10.21	3.61	4.91	6.04	.38	185	937	48	43	26
29	6.22	8.97	3.73	4.61	5.64	.41	200	930	69	35	28
30	7.22	9.79	3.83	5.15	6.11	.42	258	969	59	32	26

Dupont environmental lead studies
Los Angeles office workers DATA

Subject	On duty		Off duty	Combined exposure		DALA	Creatinine	Osmolality	ALA-Dehydrase	Urine PB	Blood PB
	Resp PB	Total PB	Total PB	Resp PB	Total PB						
1		2.17	2.86		2.62	.40	225	854	100	19	19
2		3.83	3.20		3.42	.39	138	822	70	26	21
3		3.56	3.57		3.56	.27	161	791	90	18	21
4		3.68	3.61		3.63	.31	104	783	60	15	17
5		3.68	4.21		4.02	.37	156	887	91	16	18
6		1.98	1.94		1.96	.28	146	879	109	11	12
7		2.40	3.23		2.93	.27	103	560	61	16	20
8		3.74	2.65		3.02	.29	127	895	114	13	26
9		4.06	3.39		3.62	.49	180	1005	62	30	20
10		3.74	4.05		3.93	.25	110	559	108	12	16
11		3.25	2.31		2.63	.43	212	930	106	18	19
12		3.41	4.25		3.94	.25	118	654	55	26	22
13		3.90	4.79		4.47	.33	174	981	101	27	23
14		2.57	2.50		2.53	.45	235	725	78	27	23
15		3.29	2.07		2.49	.41	215	993	101	17	16
16		3.10	2.40		2.64	.27	99	763	100	13	17
17		2.18	2.08		2.11	.36	183	870	64	17	17
18		3.31	3.70		3.57	.35	146	797	118	21	18
19		4.13	3.72		3.84	.29	122	665	77	21	19
20		4.09	3.96		4.00	.31	130	840	59	20	24
21		2.72	2.87		2.81	.29	148	755	95	16	20
22		2.23	2.64		2.47	.26	117	678	143	11	13
23		2.48	3.11		2.88	.29	124	675	147	10	15
24		2.05	2.44		2.29	.33	173	679	102	17	16
25		2.01	1.88		1.93	.23	124	721	183	11	15
26		2.84	3.22		3.08	.43	130	779	108	17	19
27		1.91	1.77		1.82	.64	305	840	109	20	17
28		3.54	3.67		3.62	.44	213	963	86	18	19
29		3.85	3.81		3.82	.40	196	959	129	20	22
30		1.93	2.23		2.11	.51	148	777	39	25	40

Dupont environmental lead studies
Philadelphia cab study DATA

Subject	Smoking category (1)	Age	Years of service	Water sample PB content
1	1	37	8	
2	3	30	15	
3	6	55	21	
4	3	51	17	
5	0	61	15	
6	3	40	11	
7	2	52	8	
8	0	45	23	
9	0	54	24	
10	4	53	21	
11	3	47	5	
12	0	43	19	
13	0	53	15	
14	6	57	18	
15	3	56	19	
16	3	64	29	
17	0	60	24	
18	3	54	20	
19	3	47	22	
20	3	40	5	
21	3	38	4	
22	0	54	19	
23	0	50	19	
24	6	49	22	
25	4	48	22	
26	3	40	7	
27	1	48	24	
28	0	60	29	
29	3	56	27	
30	4	45	18	

(1) Number	Amount of smoking
0	none
1	once in a while but not every day
2	regularily less than 1/2 pack/day
3	1/2-1 pack/day
4	1-2 packs/day
5	more than 2 packs/day
6	cigars

Dupont environmental lead studies
Starke, Florida DATA

Subject	Smoking category (1)	Age	Years of service	Water sample PB content
1	4	48	23	.9
2	0	34	15	.3
3	0	55	16	.6
4	3	57	–	4.0
5	6	41	20	.1
6	3	48	4	.4
7	6	48	22	.3
8	4	55	16	.5
9	0	63	19	1.2
10	1	56	19	.4
11	0	48	21	.1
12	0	58	22	1.6
13	0	55	17	.1
14	0	46	20	.1
15	4	45	19	.1
16	0	54	22	2.9
17	3	55	20	1.1
18	4	57	20	.1
19	0	48	22	4.2
20	3	48	20	.5
21	4	49	19	.1
22	4	41	22	.5
23	0	44	20	.2
24	6	42	20	.4
25	3	38	2	.1
26	3	43	20	3.6
27	6	43	16	.6
28	4	58	20	1.0
29	4	46	14	.6
30	4	50	22	1.1

(1) Number	Amount of smoking
0	none
1	once in a while but not every day
2	regularily less than 1/2 pack/day
3	1/2-1 pack/day
4	1-2 pack/day
5	more than 2 packs/day
6	cigars

Dupont environmental lead studies
Barksdale, Wisconsin DATA

Subject	Smoking category (1)	Age	Years of service	Water sample PB content
1	0	61	33	3.6
2	6	46	20	6.6
3	3	62	30	1.9
4	3	57	29	.2
5	0	58	29	.7
6	2	63	28	5.1
7	3	55	34	.2
8	3	26	5	.8
9	0	43	22	1.2
10	6	62	20	5.3
11	2	46	20	1.1
12	6	58	19	1.0
13	0	49	19	.4
14	3	44	17	.1
15	0	49	17	27.0
16	0	54	17	2.5
17	2	51	16	1.7
18	0	61	16	.3
19	0	41	15	2.7
20	3	61	13	.8
21	0	63	12	.7
22	0	43	8	.4
23	3	31	5	2.6
24	0	26	5	42.0
25	0	46	4	1.0
26	2	57	4	1.0
27	3	63	35	4.8
28	6	50	35	.9
29	2	51	25	30.0
30	3	62	21	3.0

(1) Number	Amount of smoking
0	none
1	once in a while but not every day
2	regularily less than 1/2 pack/day
3	1/2-1 pack/day
4	1-2 pack/day
5	more than 2 packs/day
6	cigars

Dupont environmental lead studies
Los Angeles cab study DATA

Subject	Smoking category (1)	Age	Years of service	Water sample PB content
1	–	63	34	1.2
2	0	53	30	1.3
3	0	62	25	2.3
4	0	60	25	.7
5	0	57	24	.5
6	3	54	25	2.8
7	4	51	24	.7
8	0	57	24	1.2
9	0	45	21	.2
10	3	55	20	1.3
11	2	41	19	1.6
12	3	48	18	1.6
13	0	62	17	.5
14	0	41	16	2.7
15	6	53	15	1.2
16	0	60	13	1.3
17	3	55	12	6.0
18	0	39	14	2.1
19	5	53	12	1.3
20	0	56	12	.8
21	0	44	11	1.1
22	4	50	11	.6
23	3	42	10	.9
24	3	43	9	.9
25	0	33	8	.8
26	4	32	7	2.7
27	3	29	6	.6
28	0	47	6	.5
29	3	36	6	1.8
30	3	32	6	1.3

(1) Number	Amount of smoking
0	none
1	once in a while but not every day
2	regularily less than 1/2 pack/day
3	1/2-1 pack/day
4	1-2 packs/day
5	more than 2 packs/day
6	cigars

Dupont environmental lead studies
Los Angeles office workers DATA

Subject	Smoking category (1)	Age	Years of Service	Water sample PB content
1	3	28	8	4.0
2	0	41	16	14.2
3	3	24	2	3.3
4	3	55	31	9.4
5	0	45	5	.6
6	0	59	23	.9
7	0	55	34	.9
8	1	30	5	3.4
9	1	28	4	2.6
10	0	60	23	2.3
11	0	22	3	2.7
12	2	60	25	2.9
13	6	45	5	2.6
14	5	46	24	.6
15	3	22	1	1.1
16	0	54	30	.4
17	3	42	10	1.3
18	0	65	30	1.8
19	4	22	4	4.8
20	6	27	5	14000.0
21	0	49	21	.2
22	0	34	16	1.9
23	0	63	42	1.3
24	6	46	20	.6
25	6	41	18	.3
26	4	65	18	1.2
27	3	30	10	.8
28	6	55	18	4.3
29	0	58	34	.7
30	4	55	15	6.1

(1) Number	Amount of smoking
0	none
1	once in a while but not every day
2	regularily less than 1/2 pack/day
3	1/2-1 pack/day
4	1-2 packs/day
5	more than 2 packs/day
6	cigars

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ATTACHMENT 5

Personal Exposure Sampling - Toronto

The EPA estimated personal exposures to manganese that would result from the use of HiTEC 3000 (Methylcyclopentadienyl manganese tricarbonyl, MMT) in unleaded gasoline.[1] Their estimate was based on use of carbon monoxide (CO), a gas, as a surrogate for airborne manganese, a particulate. Using a gas as a surrogate for manganese is inappropriate because CO remains airborne until it undergoes chemical change or it is absorbed or adsorbed. Particulates, however, are removed from the air by settling, impaction and precipitation. The model as developed by EPA led to a high degree of uncertainty, leading to the erroneous conclusion that a rather large segment of the population could potentially be exposed to significant amounts of manganese from HiTEC use.

Ethyl therefore undertook a program to sample personal exposures to manganese of inhabitants of the Toronto, Ontario metropolitan area. HiTEC 3000 is allowed for use at levels about twice those requested by Ethyl for use in unleaded gasoline in the U.S. This allows for the measurement of actual exposures rather than estimating exposures utilizing various algorithms.

Sampling was carried out utilizing SKC Model 224-PCXR3 Constant-Flow Air Sample Pumps and 37 mm diameter Millipore mixed-cellulose ester filters (nominal pore size 0.8 um) with polycarbonate "cassette" holders. These battery operated pumps are designed for performing personnel sampling in the workplace. Chargers were provided to the individuals being monitored to allow the pumps to continue uninterrupted service. Similar filters with nominal pore size of 3.0 um were shown to be better than 99% efficient in trapping lead aerosols from automobiles burning gasoline with tetraethyl lead.[2] The lead and manganese particulates have similar mass median equivalent diameters.[3]

The individuals monitored were instructed to carry the samplers with them when outdoors and to keep them nearby when indoors. Samples were collected for approximate 7-day periods in most cases. Sampling was carried out from 2/4/91 to 2/19/91. The weighted average amount of manganese in gasoline during this time was 0.039 gram manganese per gallon.[4]

Presumably, the most highly exposed group of individuals to manganese from HiTEC 3000 would be those that spend large amounts of time in traffic. Therefore, several taxicab drivers were included in the study. Others included office workers from various locales in and around Toronto. In all cases, exposures were quite low, well under the EPA's proposed Reference Concentration (R_fC) for airborne manganese (0.4 ug/m^3).

The results of the sampling show that "office workers" had a mean exposure to airborne manganese of 0.013 ug/m^3 with a standard deviation of 0.009 (Table 1). Exposures for this group ranged from 0.002 to 0.049 ug/m^3 air. Exposures at the 99th percentile for these workers (mean + 3 times the standard deviation) would only be 0.040 ug/m^3, an order of magnitude below the proposed R_fC. It should be noted that one sample was a rare event, i.e. at a level above this 99th percentile (0.049 ug/m^3).

Taxi drivers (Table 2) had a mean exposure of 0.035 ug/m^3 with a standard deviation of 0.010 ug/m^3. Exposures ranged from 0.015 to 0.049 ug/m^3. The 99th percentile exposure for this group of individuals is only 0.065 ug/m^3. Taxi drivers are a population subgroup that would be expected to have some of the highest exposures to HiTEC 3000 related airborne manganese. Even this subpopulation had exposures well below the proposed R_fC, and even at the 99th percentile.

In addition to the personal exposure samples, a few samples were taken to determine levels of manganese in various microenvironments. The microenvironments investigated include those with potential for high manganese levels from HiTEC 3000, i.e. an underground parking garage and a semi-enclosed hotel motor courtyard. The levels averaged about 0.25 ug/m^3 in the parking garage and about 0.28 ug/m^3 in the motor courtyard. These samples were not taken 24 hours/day, but were taken during the "peak hours" of activity, about 8 hours/day. Therefore, they represent maximum exposures in these areas. The large variation in the levels reported in the parking garage reflects differences in various areas of the parking garage.

We can make a very conservative estimate of possible exposures for people who work in these microenvironments by assuming that their "on-duty" exposures are equal to the average microenvironment air level (0.265 ug/m^3) and their "off-duty" exposures are equal to the mean of the non-cab samples, 0.013 ug/m^3. The average 24-hour exposure for these people would be:

$$\frac{0.265 \times 8 + 0.013 \times 16}{24 \text{ hour}} = 0.097 \text{ ug/m}^3$$

This is about a fourth of the EPA's proposed R_fC for manganese. However, if we assume a 40 hour work week, the long-term average exposure would be somewhat less. It would be equal:

$$\frac{0.265 \times 40 + 0.013 \times (7 \times 24-40)}{24 \times 7} = 0.073 \text{ ug/m}^3$$

This is well below the EPA's proposed R_fC. These estimates are extremely conservative as no employee would likely spend 8-hours a day in the garage in the high exposure area.

The sampling data clearly show that exposures of the general population to airborne manganese from HiTEC 3000 use in unleaded gasoline would be well within levels believed to be safe by standard setting groups including the U.S. EPA (R_FC = 0.4 ug/m^3)[1], the World Health Organization (1 ug/m^3)[5], the U.S. Agency for Toxic Substances and Disease Registry (2 ug/m^3)[6] and Ontario, Canada (10 ug/m^3 for 24 hours)[7].

G. D. Pfeifer

GDP:cr
Attachments
106GDP91

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2. Konospinski, V. J. and Upham, J. B., Commuter Exposure to Atmospheric Lead, Arch. Environ. Health, 14 (1967), 589-593.

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4. Personal Communication from Canadian Petroleum Products Institute to D. C. Wilson, President Ethyl Canada.

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TABLE 1

TORONTO OFFICE WORKERS-EXPOSURE TO AIRBORNE MANGANESE
UG Mn/CUBIC METER

SAMPLE	WEEK 1	WEEK 2	MILAGE-HOME TO DOWNTOWN	MODE OF TRAVEL
BM1	0.018		1.5	CAR
BM2	0.002		50	CAR(12), TRAIN(36)
BM3	0.021		1.5	SUBWAY/WALK
BM4	0.012		0.25	WALK
BM5	0.007		3	CAR
BM6		0.007	18	CAR
BM7		0.048	7	SUBWAY
BM8		0.031	10	BUS
BM9		0.005	1	BUS
BM10		0.027	6	CAR
BR1A	0.020		0	
BR2A	0.016		0	
BR1B		0.005	0	
BR2B		0.003	0	
SO1	0.007	0.007		CAR
SO2	0.007	0.010	>10	CAR
SO3	0.018	0.019	5.5	CAR
SO4		0.014		CAR
SO5	0.009	0.006	>10	CAR
[illegible]	0.010	0.008	>10	CAR
[illegible]2	0.012	0.009	>10	CAR
EC3	0.016	0.012	9.5	
DR1	0.021	0.009	4	CAR
DR2	0.013	0.007	4	CAR
AVERAGE	0.013	0.013		
STD DEV.	0.006	0.011		
N	16	17		

OVERALL AVERAGE	0.013
STD DEV.	0.009
N	33

TABLE 2

TORONTO CAB DRIVERS-PERSONAL EXPOSURES TO MANGANESE

	UG Mn/CUBIC METER WEEK 1	WEEK 2	MILAGE-HOME TO DOWNTOWN	MODE OF TRAVEL
CAB1	0.046	0.036	8.5	CAR
CAB2	0.038	0.040	>10	CAR
CAB3	0.049		1.5	CAR
CAB5	0.039	0.015	1.75	CAR
CAB6	0.023	0.026		CAR
CAB7		0.040	5.5	CAR
AVERAGE	0.039	0.031		
STD DEV.	0.009	0.010		
N	5	5		

OVERALL AVERAGE	0.035
STD DEV.	0.010
N	10

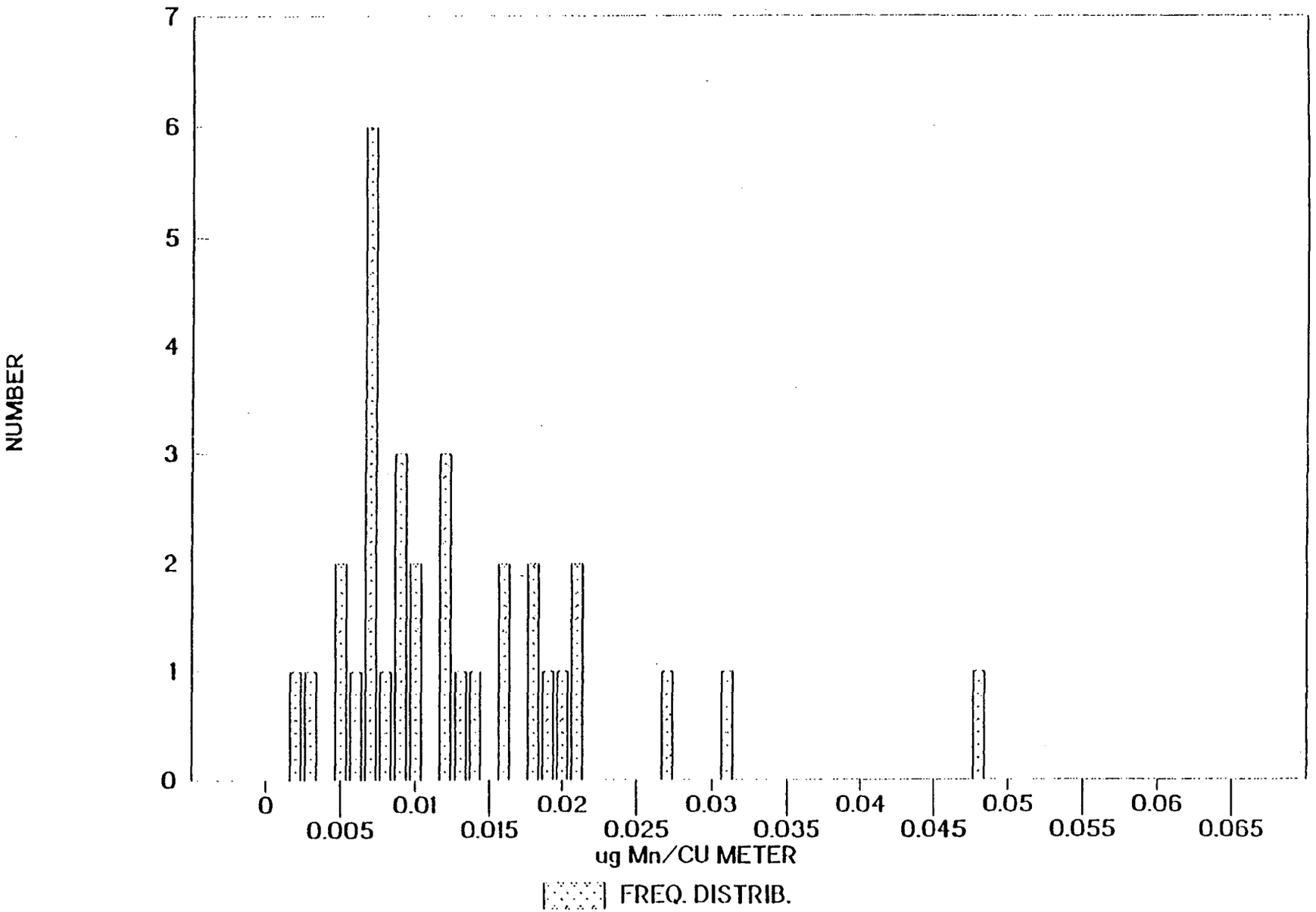
NOTES:
CAB 3-DID NOT PARTICIPATE THE SECOND WEEK
CAB 4-DECIDED NOT TO PARTICIPATE

TABLE 3
AIRBORNE Mn LEVELS-MICROENVIRONMENTS (uG/CU METER)
TORONTO FEBRUARY 1991

	WEEK 1	WEEK 2
UNDERGROUND PARKING GARAGE	0.41	0.093
HOTEL MOTOR COURTYARD	0.325	0.231

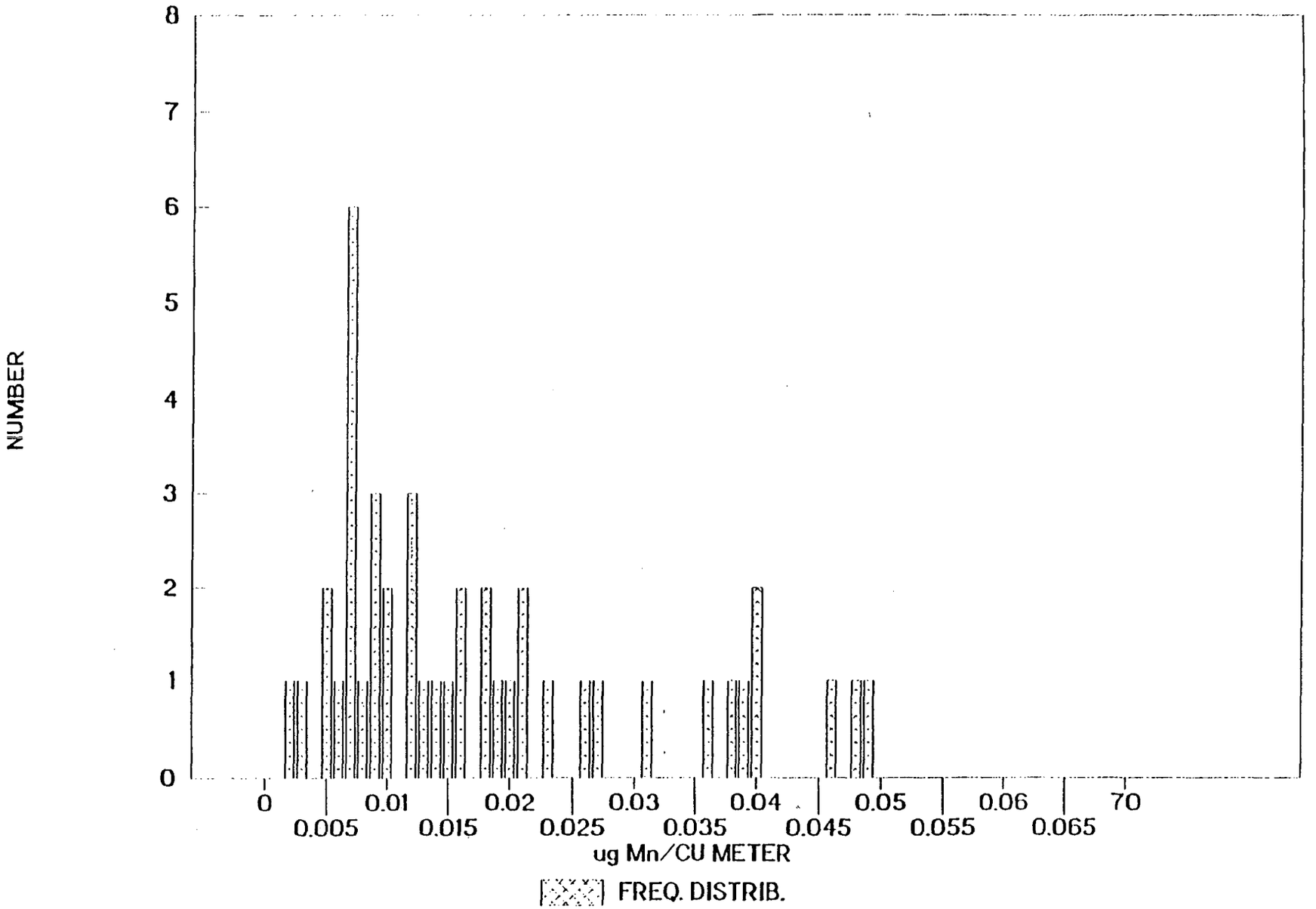
FREQUENCY DISTRIBUTION NON-CAB

TORONTO AIR SAMPLES



FREQUENCY DISTRIBUTION ALL

TORONTO AIR SAMPLES



ATTACHMENT 6

Health and Environmental Risks and Benefits from Use of MMT in Unleaded Gasoline

by

Chris Whipple, Ph.D.

Clement International Corporation

San Francisco

presented at the

EPA Manganese/MMT Conference and Workshop

Raleigh

March 12-15, 1991

Revised June 20, 1991

Health and Environmental Risks and Benefits from Use of MMT in Unleaded Gasoline

Background and Introduction

Ethyl Corporation submitted a waiver application on May 9, 1990 to EPA's Office of Mobile Sources (OMS) for the use in unleaded gasoline of its HiTEC® 3000 Performance Additive, methylcyclopentadienyl manganese tricarbonyl (MMT). The OMS asked EPA's Office of Research and Development (ORD) to assess the potential health risks associated with emissions resulting from the proposed MMT use. The ORD responded with a report, "Comments on the Use of Methylcyclopentadienyl Manganese Tricarbonyl in Unleaded Gasoline," issued November 1, 1990. The major effort of the ORD was a risk assessment of MMT use.

The ORD analysis indicates that MMT itself does not appear to pose significant health or environmental risks, nor do exposures to manganese at the average levels that would result from MMT use at the level of 1/32 gram manganese per gallon. The ORD report also notes that "introduction of MMT into gasoline could possibly positively affect tropospheric ozone, greenhouse gas emissions, and various crops. Reduced vehicular emissions of aromatics due to MMT use could also reduce the cancer risk associated with benzene exposures." However, potential benefits from MMT use were not considered in